Part I:

An introduction to Nano-particle particle size using light scattering : Principle & Applications

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CORDOUAN Technologies

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Nano-Materials & Nanoparticles :

- Promise of major technologic, economic, societal & environmental impacts
- Already in the field ….. And it is just the beginning!

food

Pharma

Cosmetic

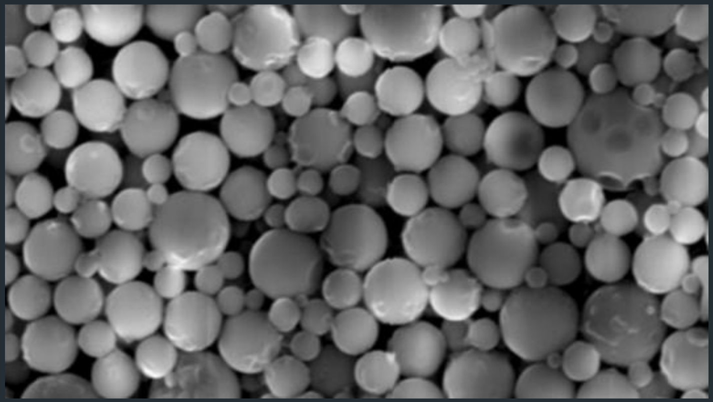
Petrol

Battery/Automotive

Environment

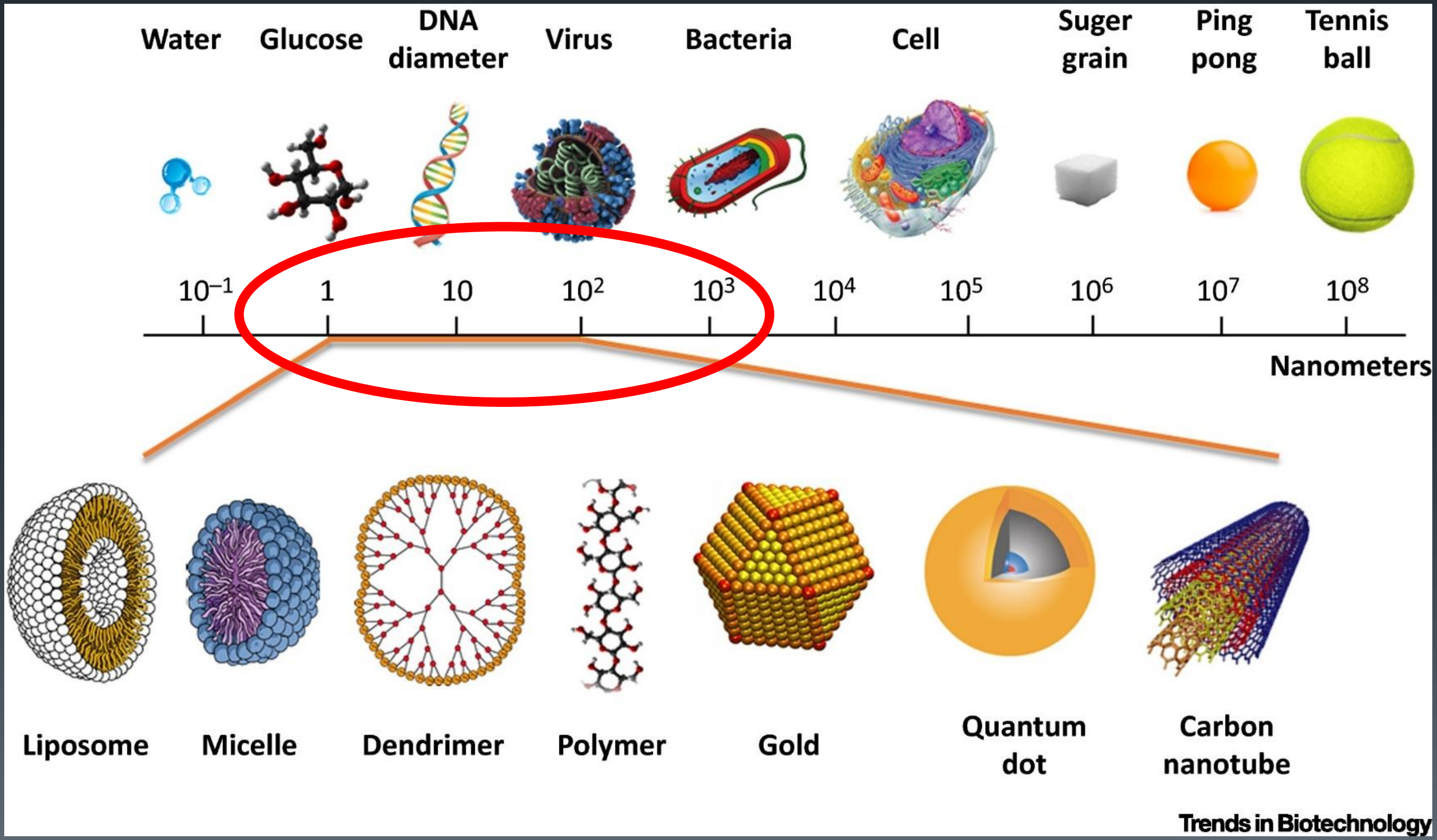
https://www.understandingnano.com/nanoparticles.html

Nano-Materials & Nanoparticles : definition and types

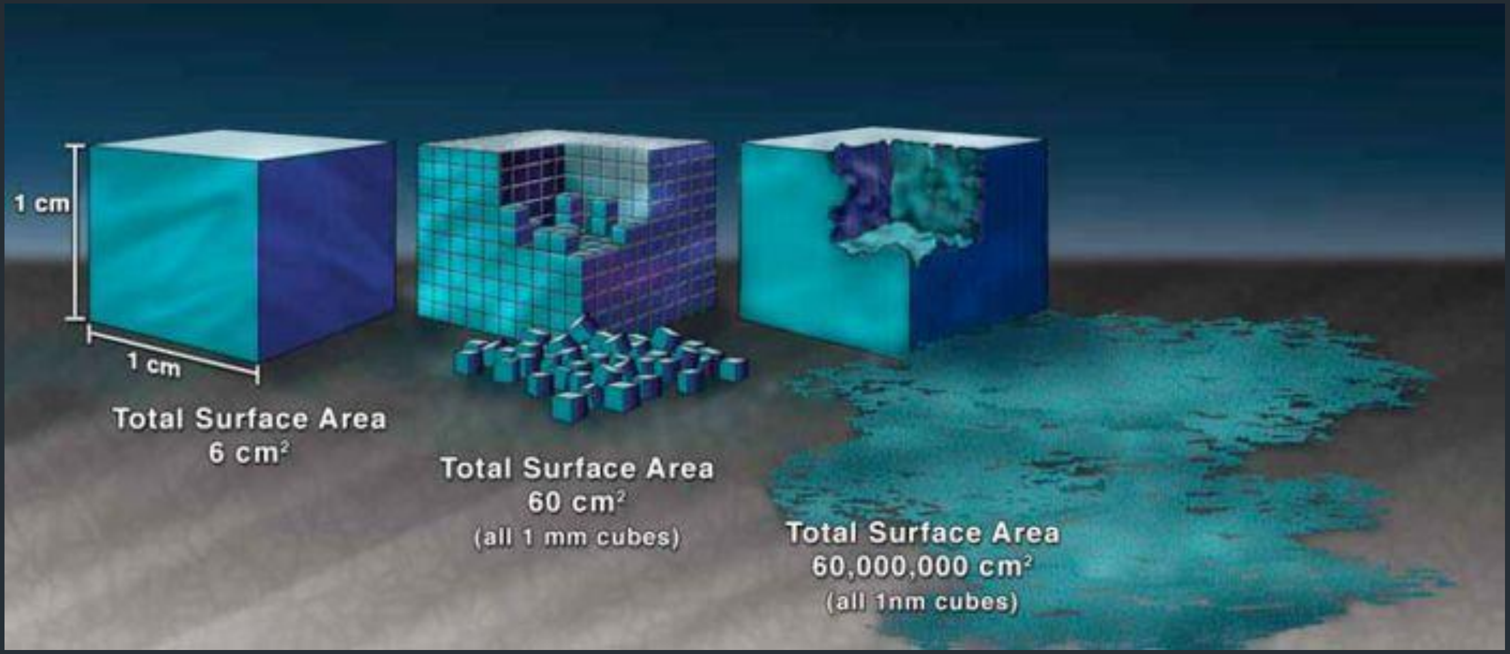


*Definition (Europe) : "A **natural, incidental or manufactured** material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the **size range 1 nm - 100 nm**"; But more generally for colloid size ranges from 1 nm to 10 µm!*

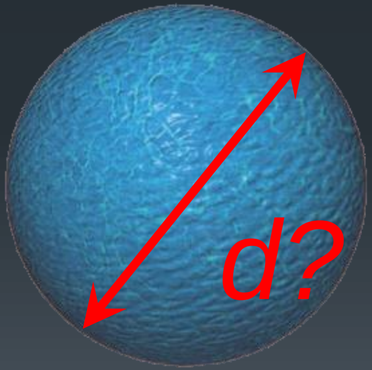
http://ec.europa.eu/environment/chemicals/nanotech/faq/definition_en.htm



Nano particle size measurement : why is it important?

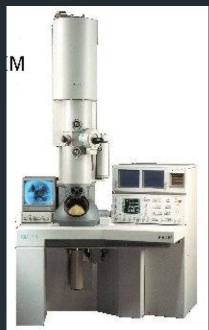


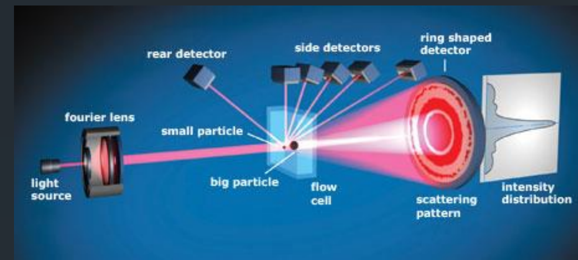
- Related to the specific surface of the particles
- Ability to penetrate membranes or interact with surface
- Aggregation and stability of suspensions
- Functionnalisation and self assembly capabilities
- Optical, mechanical and electrical properties



Many mature characterization techniques for particle size

SAXS, TEM





Laser Diffraction
(Static light scattering)

0 1 nm 100 nm 1 µm 1 mm

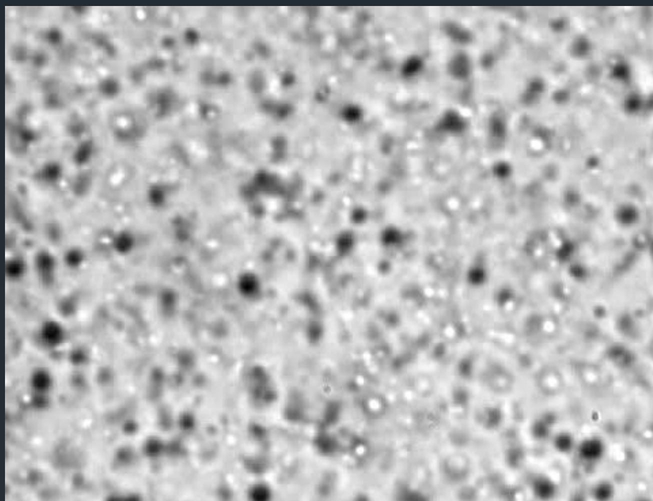
Classical Optical microscopy

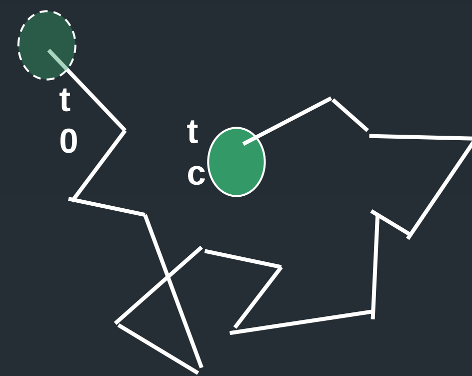
DLS: 1 nm to 10 µm

4 decades of size range!!!

DLS uses Brownian motion as a signature of particle size

Brownian motion= Random “walk”





Diffusion coefficient   time

$$< X^2(t) > \sim 2\, D\, t$$

L. BACHELIER (1901)

NPs:
hard spheres without interactions

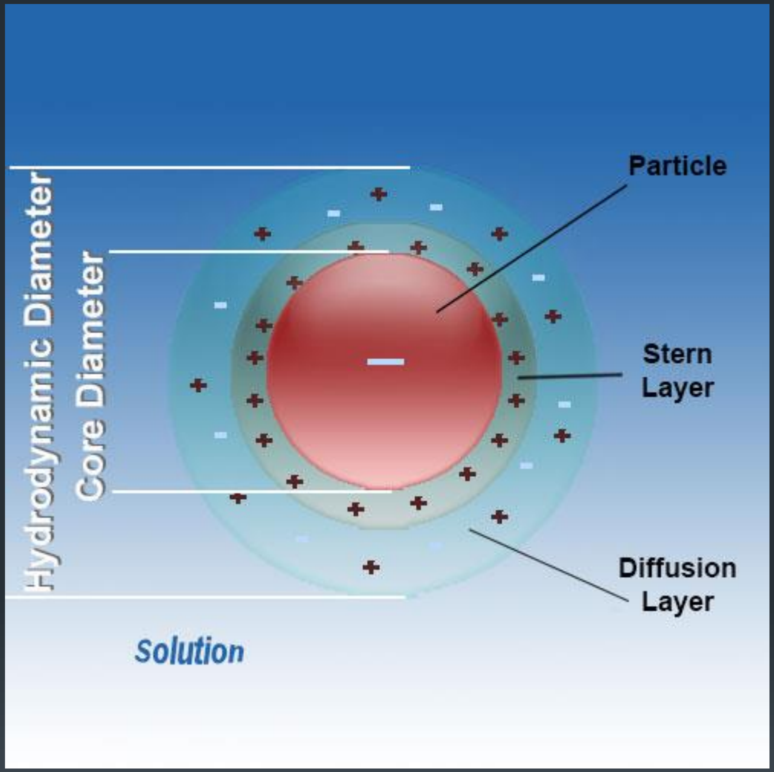
Viscosity   *Boltzmann*   *Temperature*

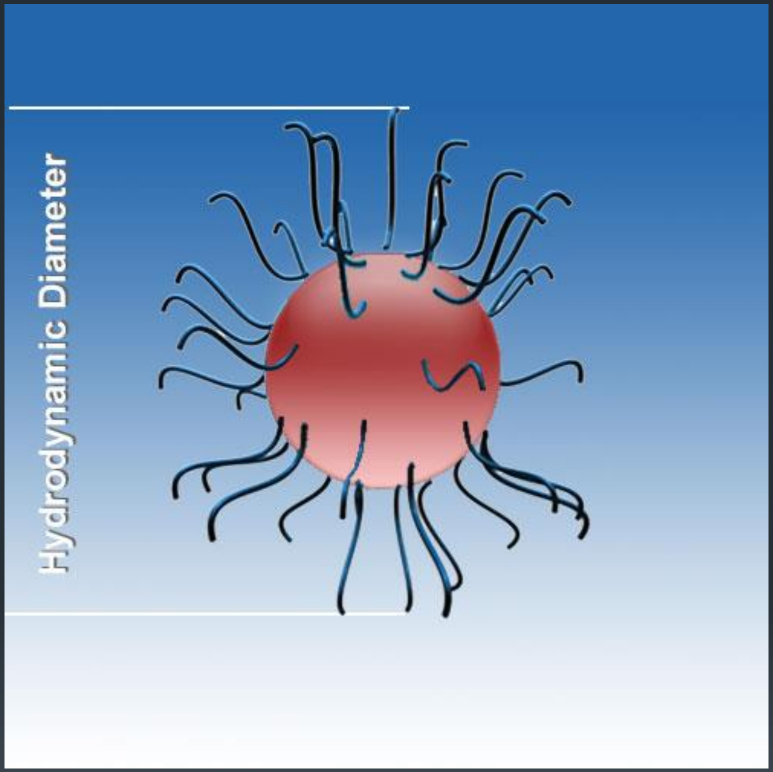
$$D = \frac{KT}{3\pi\eta\, \emptyset_H} \quad \Rightarrow \quad \emptyset_H = \frac{KT}{3\pi\eta D}$$

EINSTEIN & Stokes (1905)

Meaning of hydrodynamic diameter $\varnothing_H$

Hydrodynamic diameter = diameter of the particle **+** double layer thickness

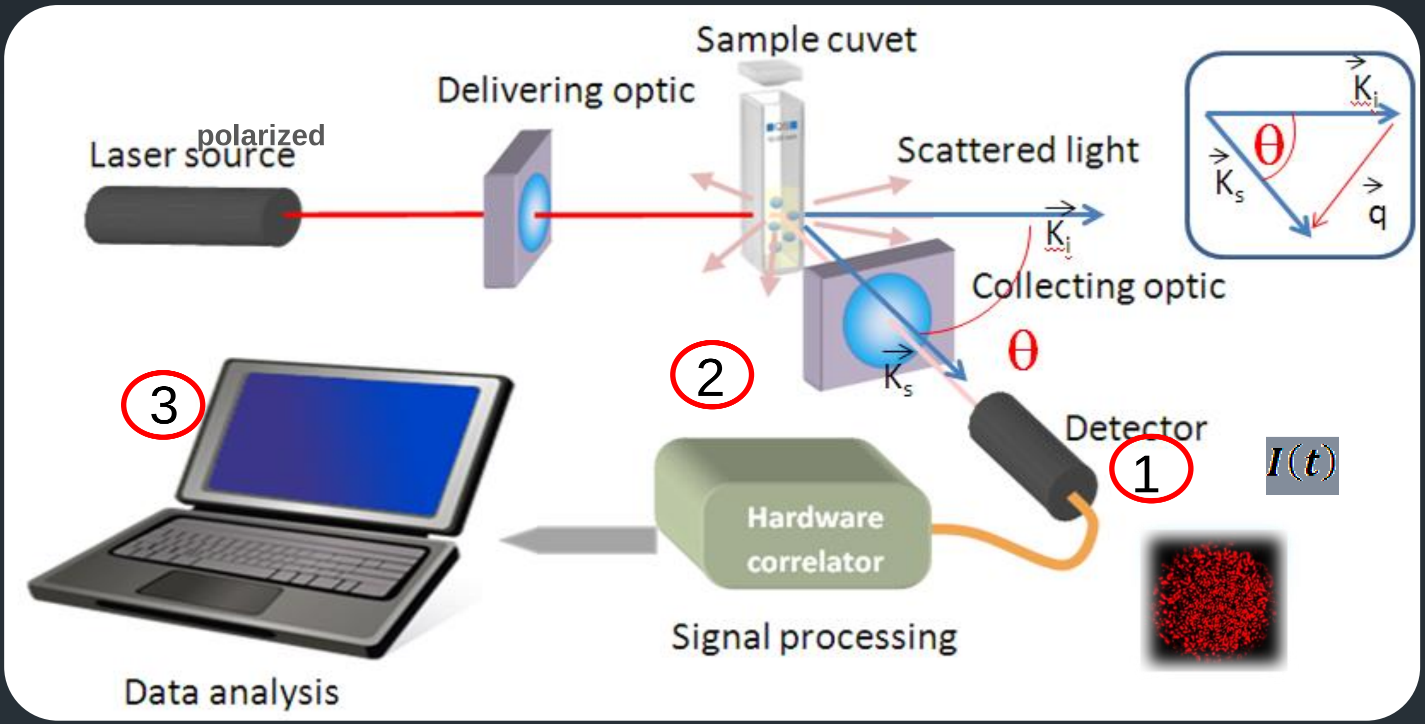


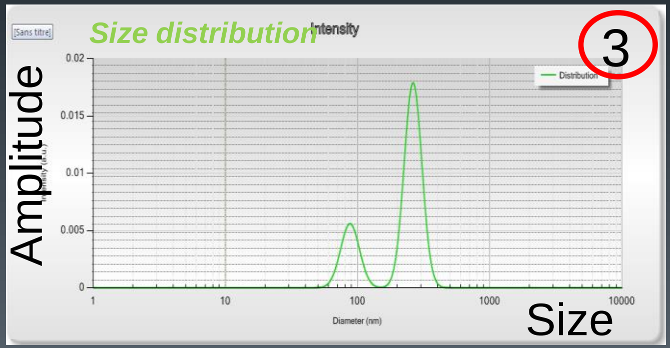


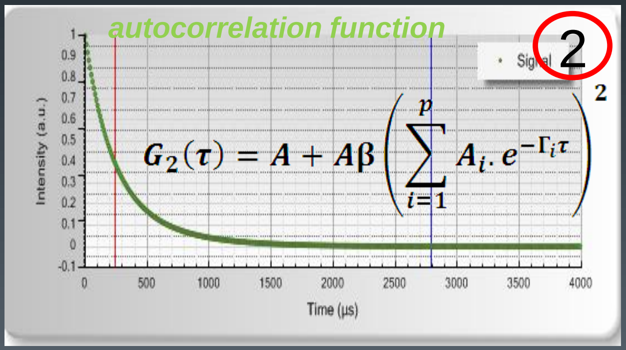
Hydrodynamic diameter is usually > Core diameter (TEM/SAXS) Value by several nm!

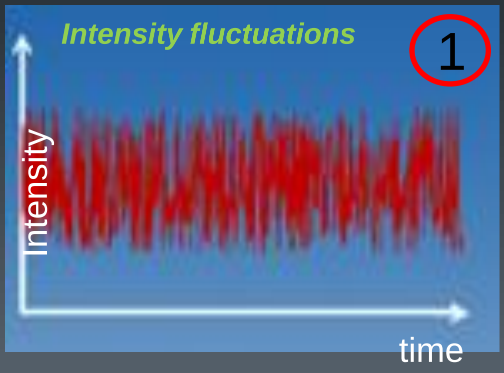
DLS measurement principle: 3 steps process

➢Measure light scattering fluctuation to probe the Brownian motion







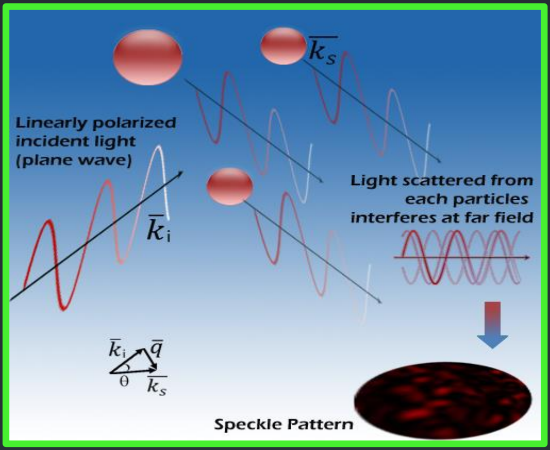


Intensity measurement and correlogram

Considering coherent electromagnetic waves scattered and measured at a specific angle (scattering vector $\mathbf{q}=\mathbf{k}_i-\mathbf{k}_s$) :

Detected field and Intensity :

EM field: $E_{tot\_detect}(\omega t)=\Sigma E_i \exp(i(\mathbf{q}.\mathbf{r}-\omega t))$



Intensity: $I(t)= E_{tot}(t) \times E_{tot}^*(t)$

Autocorrelation :

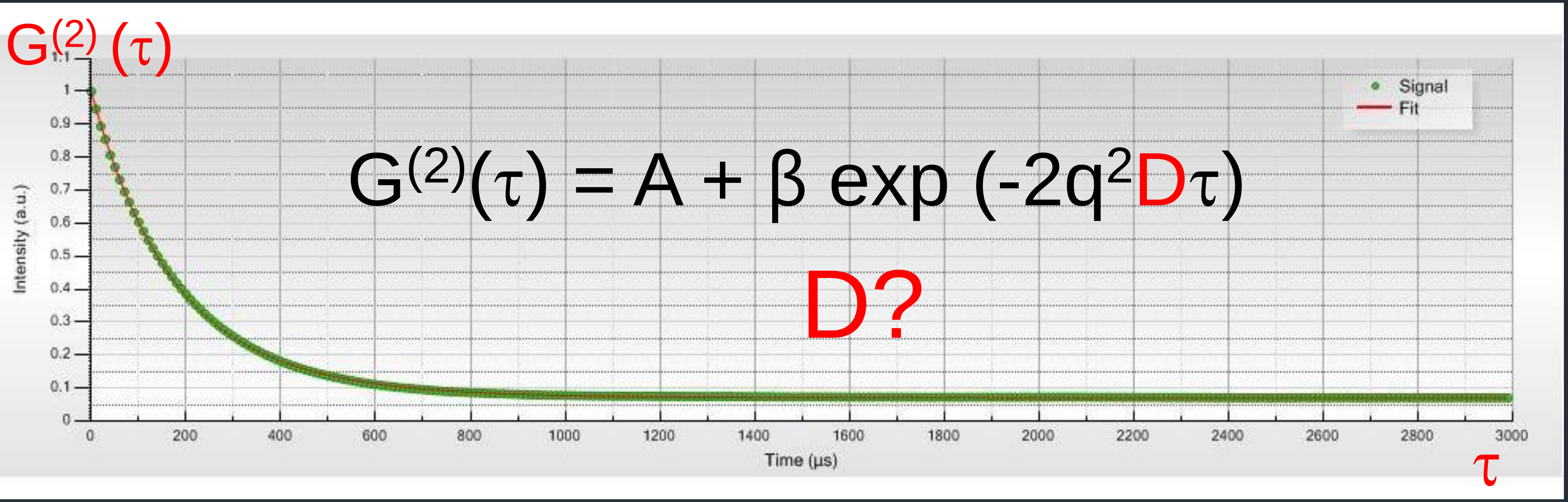
Field : $g^{(1)}(\tau) = \dfrac{<E^*(t)E(t+\tau)>}{<E^2(t)>}$

Intensity : $G^{(2)}(\tau) = \dfrac{<I(t)\,.\,I(t+\tau)>}{<I^2(t)>}$

This leads : $G^{(2)}(\tau) = A + \beta \exp(-2q^2\mathbf{D}\tau)$

with $q=\dfrac{4\pi n_0}{\lambda}\sin(\theta/2)$

Inversion problem : finding the best Mathematical fitting of the correlogram?



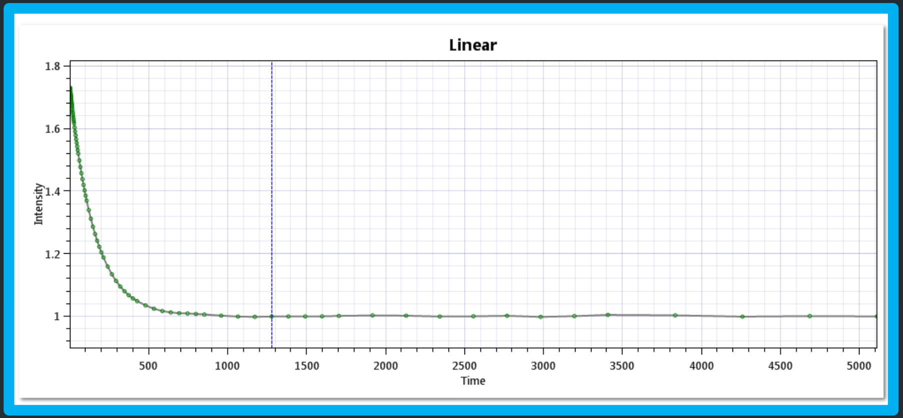
Fit leads to D, and D to the diameter of NPs $\emptyset_H$.

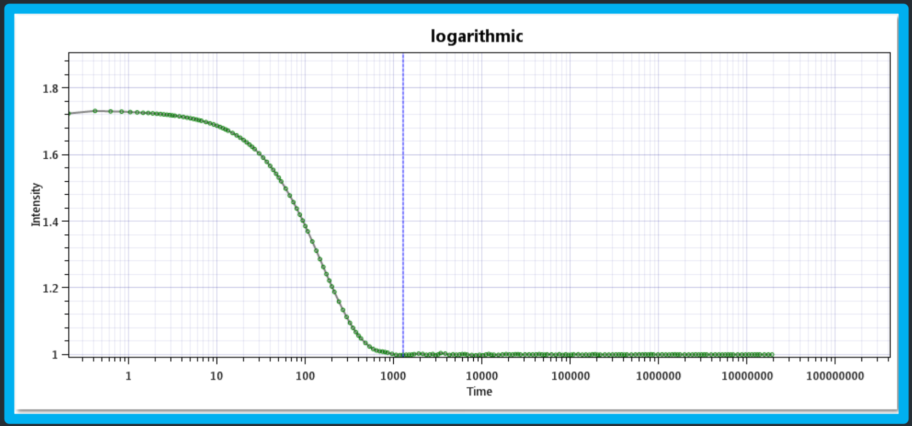
$$D \rightarrow \emptyset_H = \frac{KT}{3\pi\eta D}$$

Correlogram representation: Linear vs Logarithmic

linear correlator

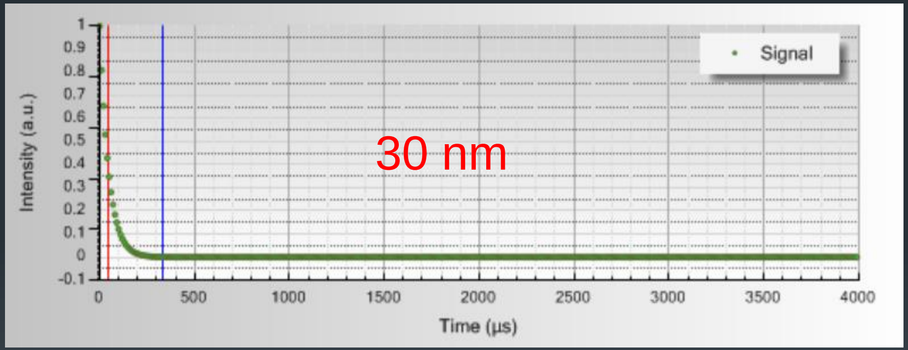
Multi-tau/Log correlator

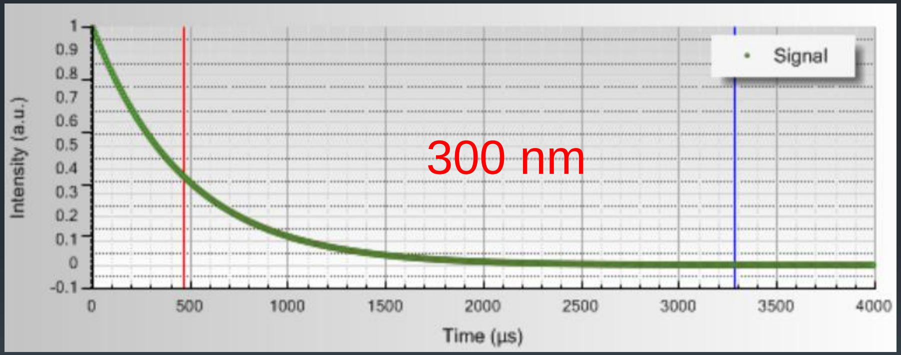


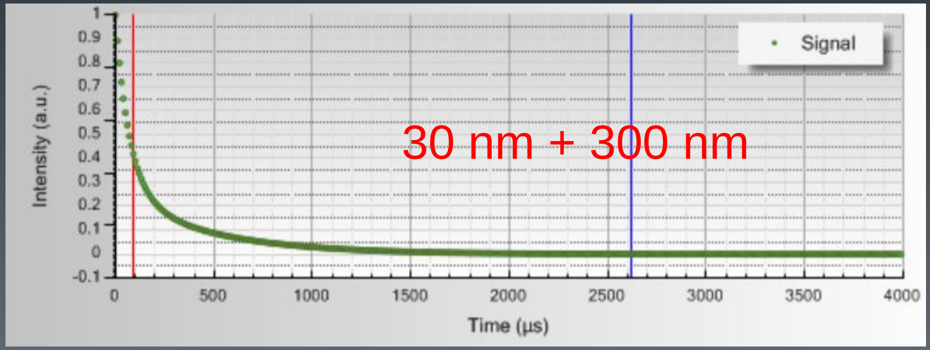


Linear time scale

Logarithmic time scale

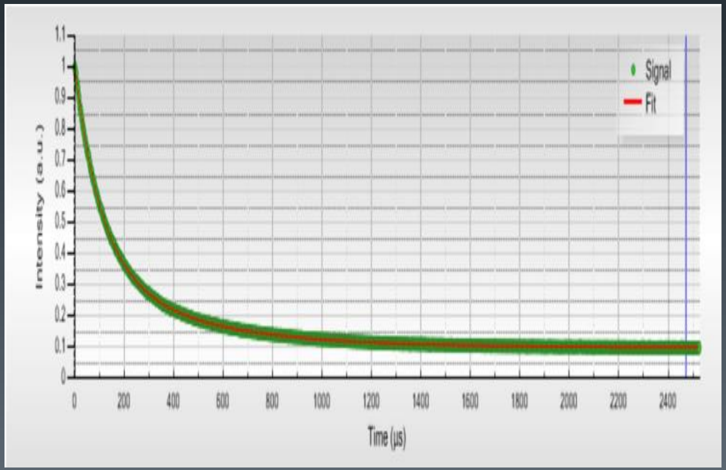


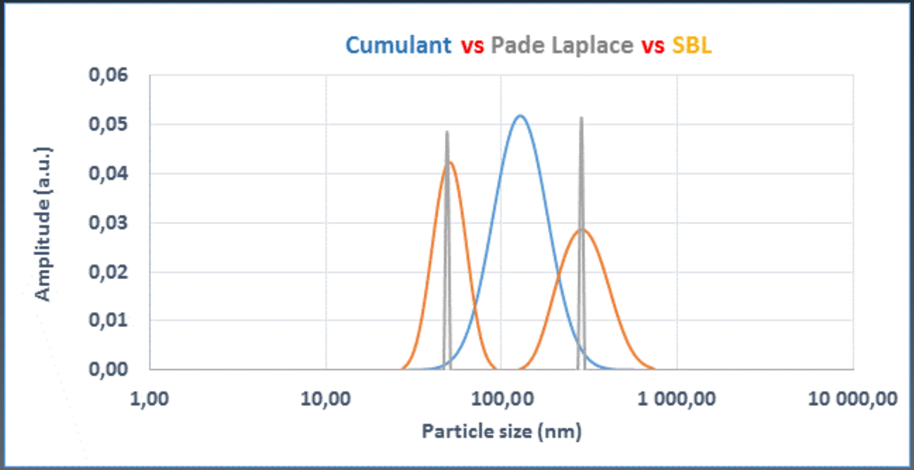




Inversion algorithms for monomodal and polymodal analysis

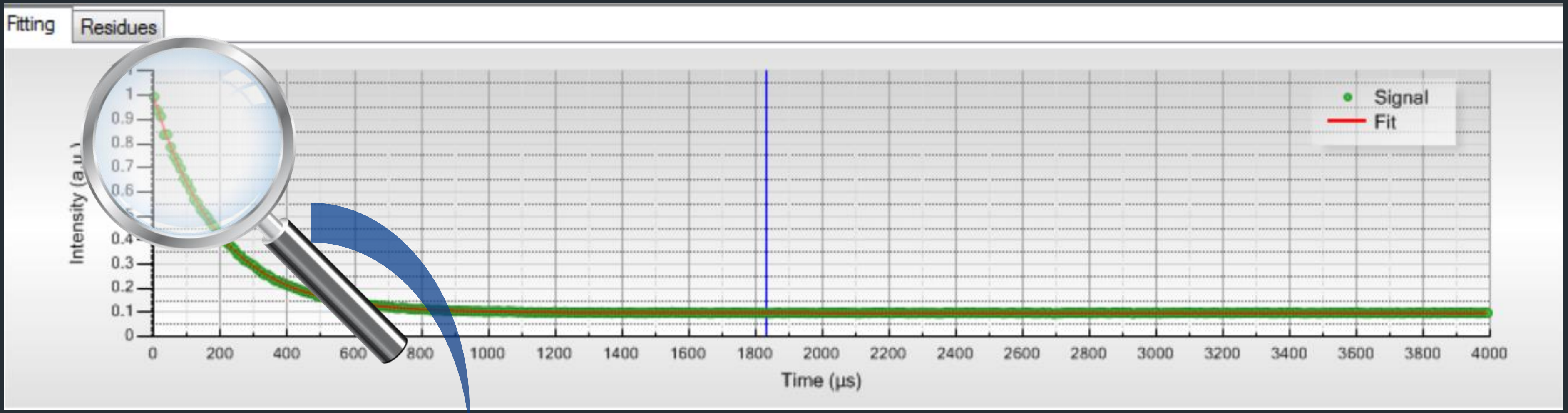
Algorithm	Number of populations	Distribution	Model
Cumulants	1 Continuous Gaussian with Zavg & PDI	Yes	$G(\tau)=A+B\,e^{-\Gamma\tau}$ $Z_{avg}=\frac{k_B T q^2}{3\pi\overline{\Gamma}};$ $Distribution\ width = Z_{avg} * \sqrt{PDI}$
Pade Laplace	Multi (up to 3) discrete	No	$G(\tau)=A+\sum_{i=1}^{250} B_i\, e^{-\Gamma_i\tau}$
SBL	Multi continuous	Yes	$G(\tau)=A+\int_0^{10\mu m} B(z)\, e^{-\Gamma(z)\tau}dz$



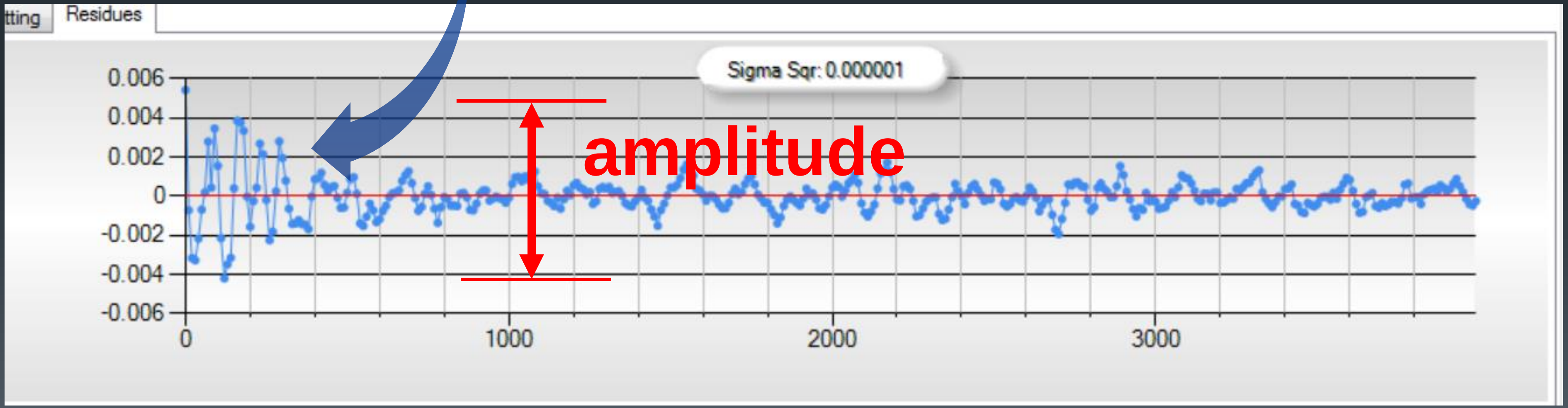


The key point of the results : the FIT and the Residues

FIT= mathematical solution given by the algorithms (red curve)

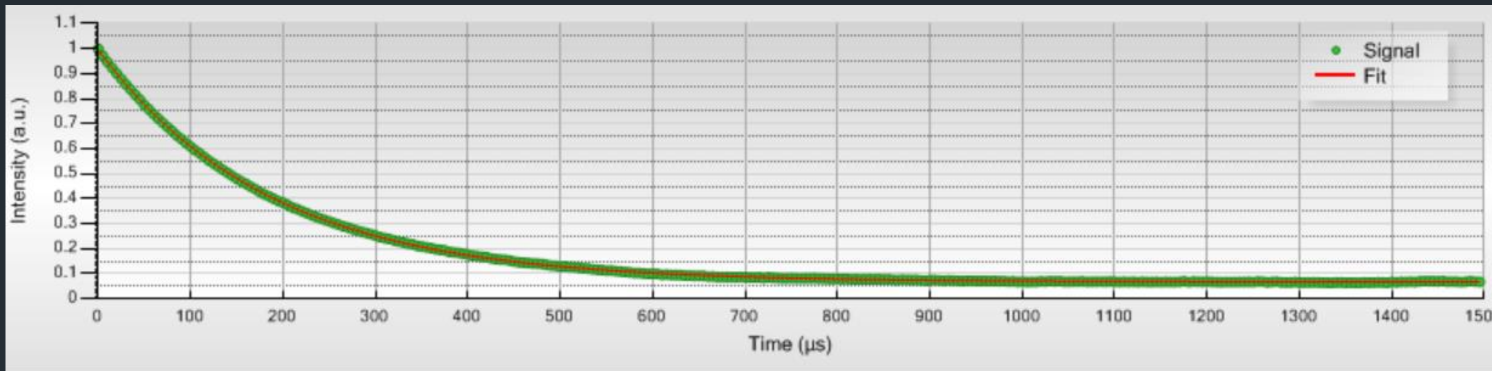


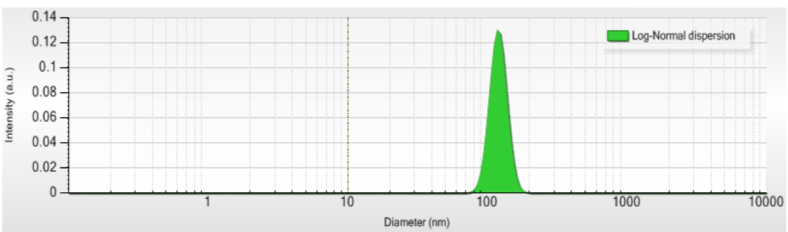
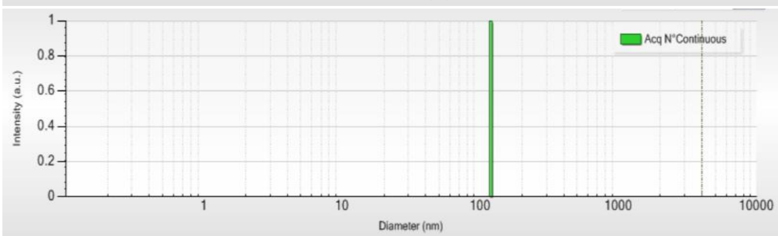
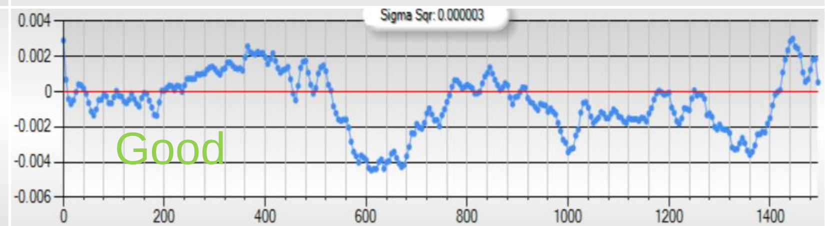
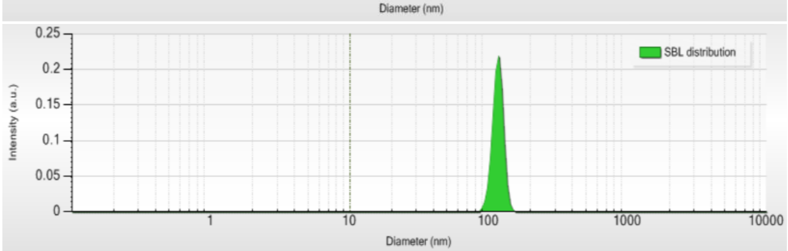
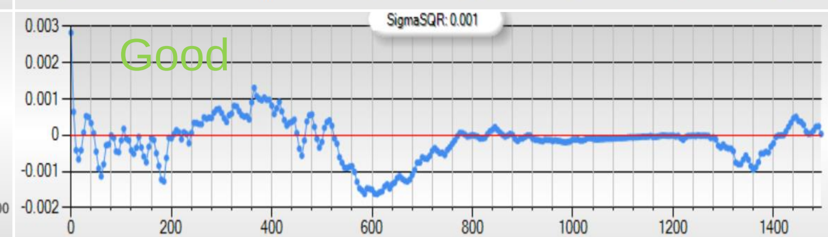
Residues = difference between Fit and measured correlogram



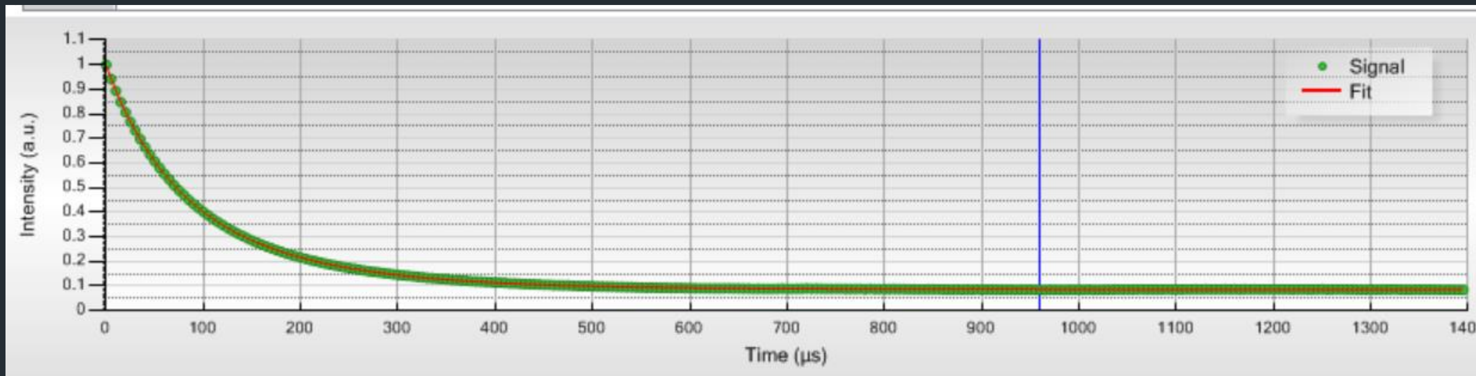
A good fit = Low amplitude (<0,01) and statistically distributed residues

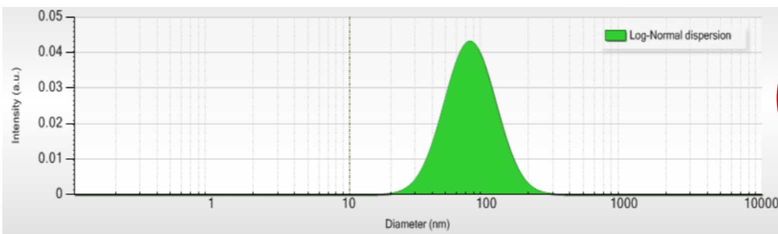
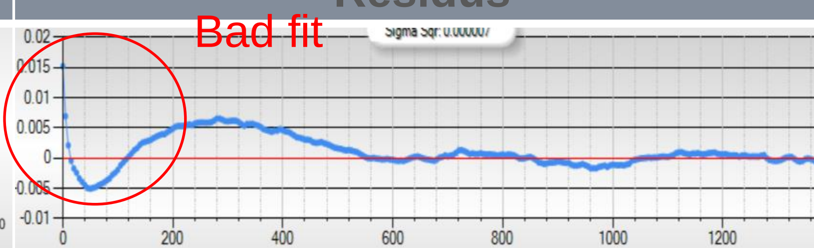
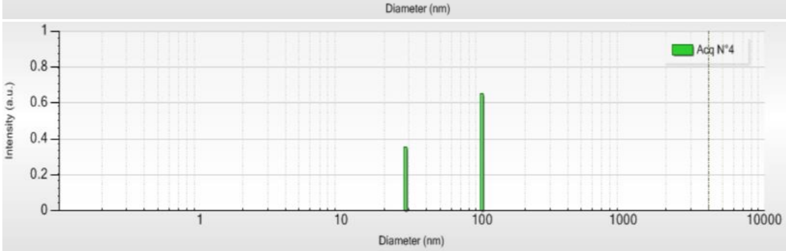
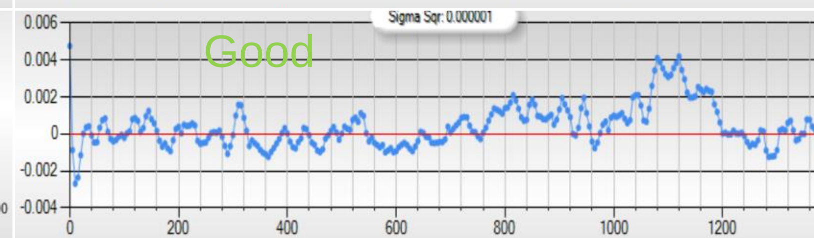
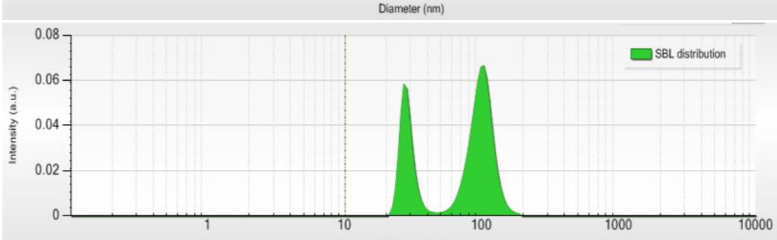
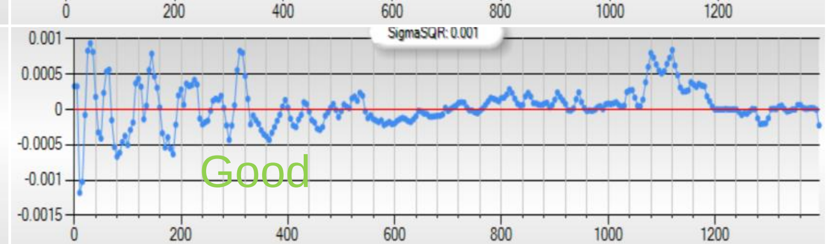
Monomodal sample (one population) 100 nm Latex NPs



Algorithm	Size	Residus
Cumulants		 Good
Pade Laplace		 Good
SBL		 Good

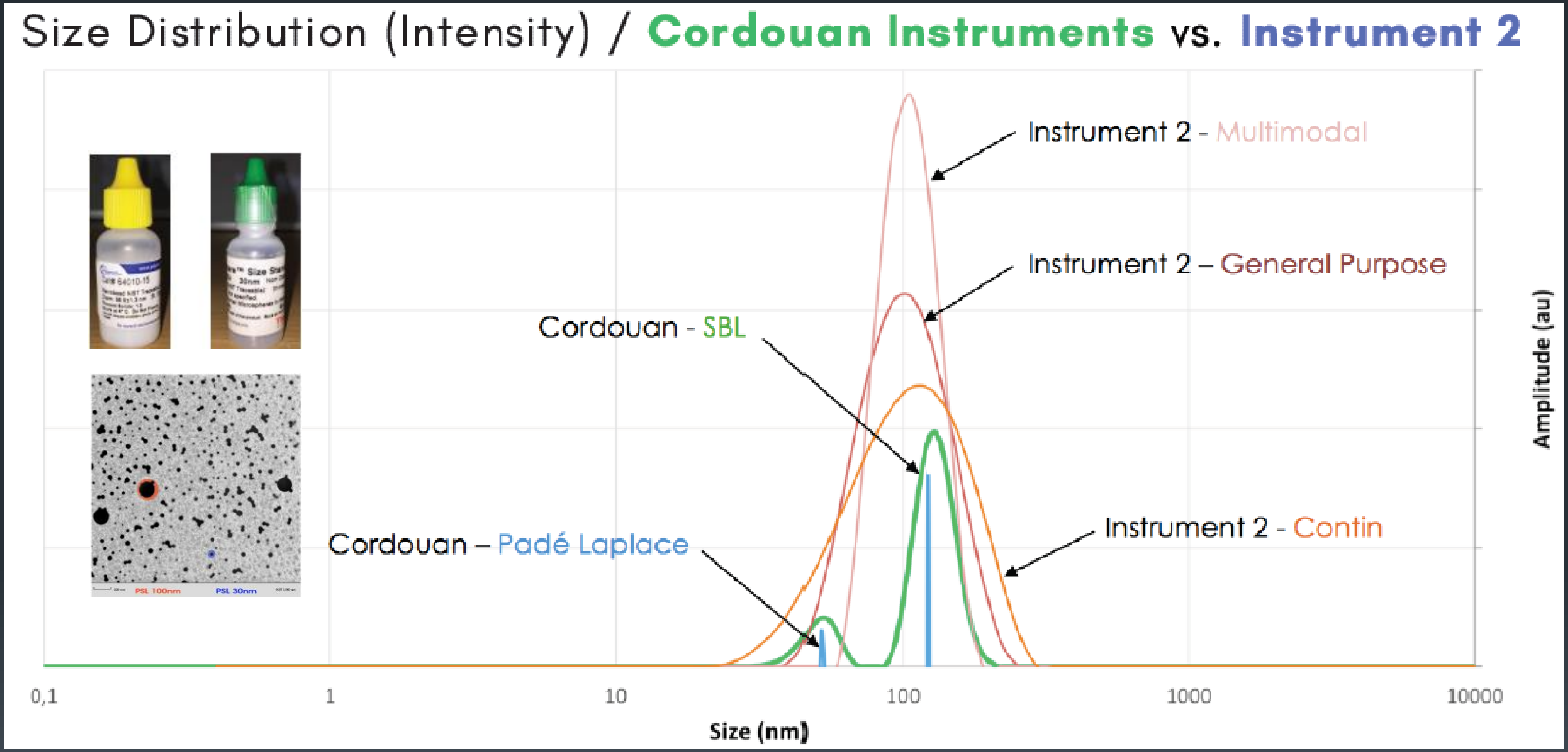
Bi-modal sample (two populations) 30 nm +100 nm Latex NPs mixture



Algorithm	Size	Residus
Cumulants		
Pade Laplace		
SBL		

Importance of powerful algorithms for high resolution measurement

30 nm + 100 nm Polystyrene latex (PSL) - unknown ratio, blindfolded sample test



Efficient algorithms make a clear difference for high resolution particle size measurement on complex samples.

Light Scattering: some useful rules of thumb:

MIE/ Rayleigh Theory

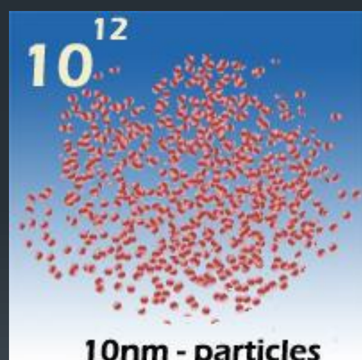
$$I_{Scatt} \sim K \,.\, I_0 \left(\frac{(n2-1)}{(n^2+2)}\right)^2 \cdot \frac{\varnothing_H{}^6}{\lambda^4}$$

Particle refractive index

Laser Wavelength

Rule of thumb #1: the scattering efficiency (cross section) of the particles is 2.3 times higher for a laser wavelength @532 nm than that of a laser @656 nm

***Rule of thumb #2*:** light intensity scattered by 10nm spherical particles is 10^6 (one million!) times lower than for 100 nm particles,



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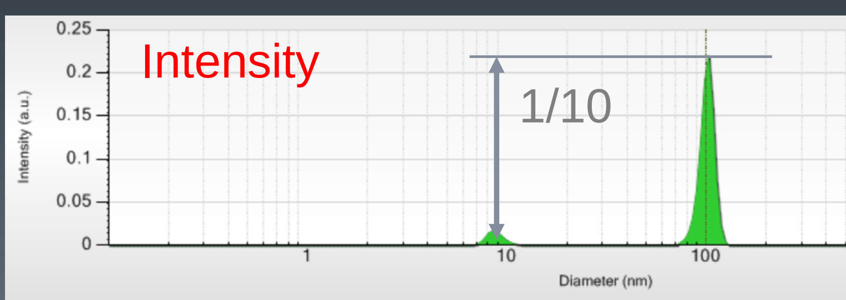
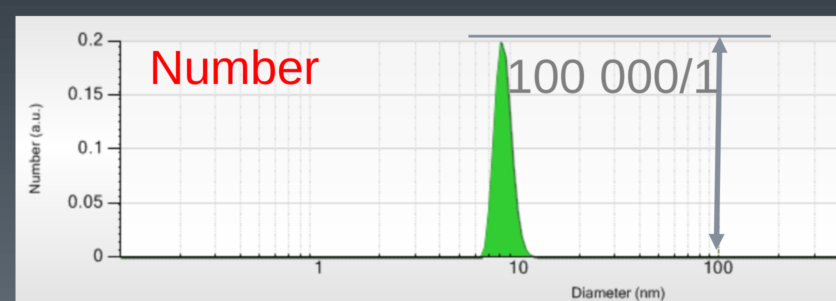
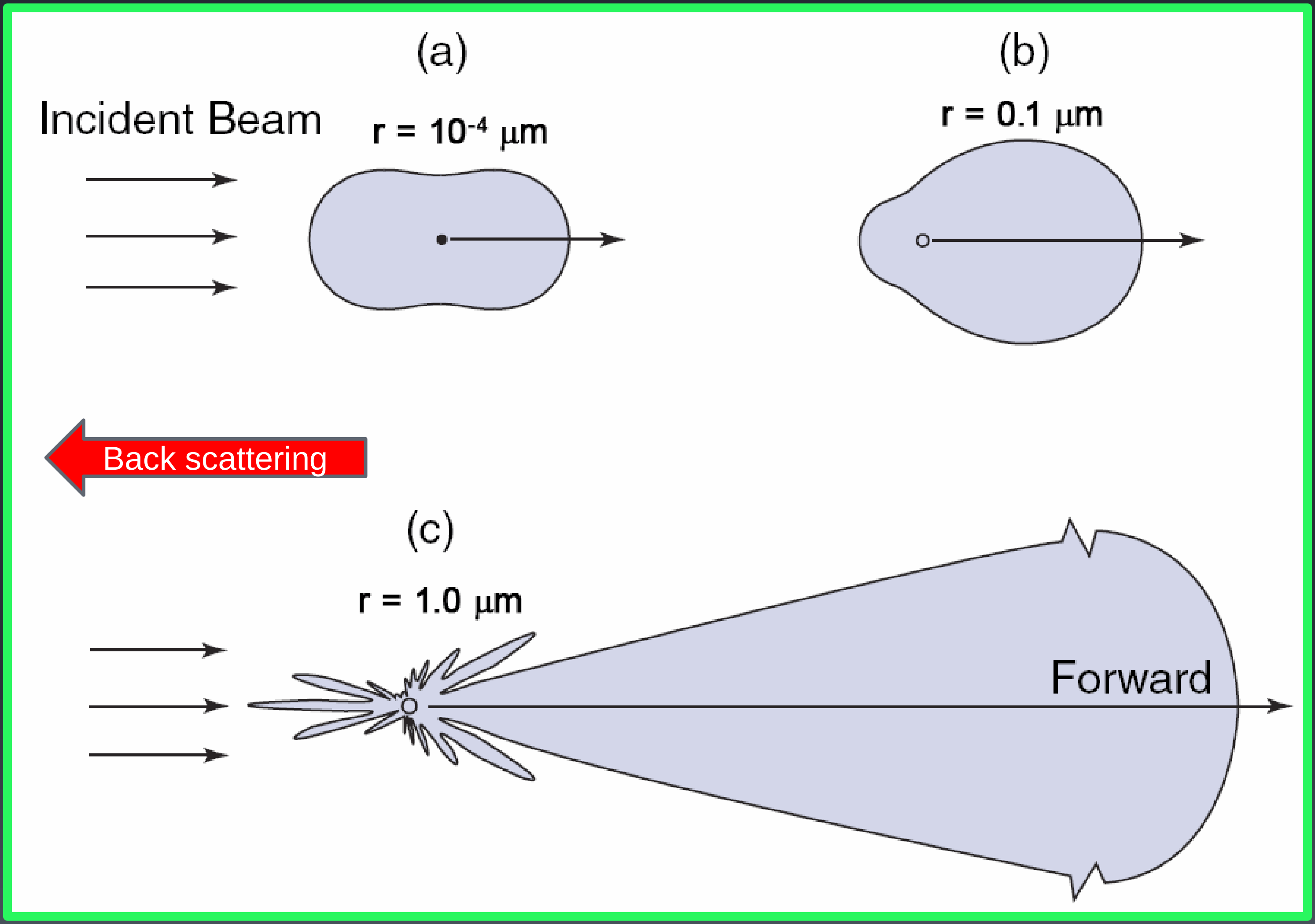




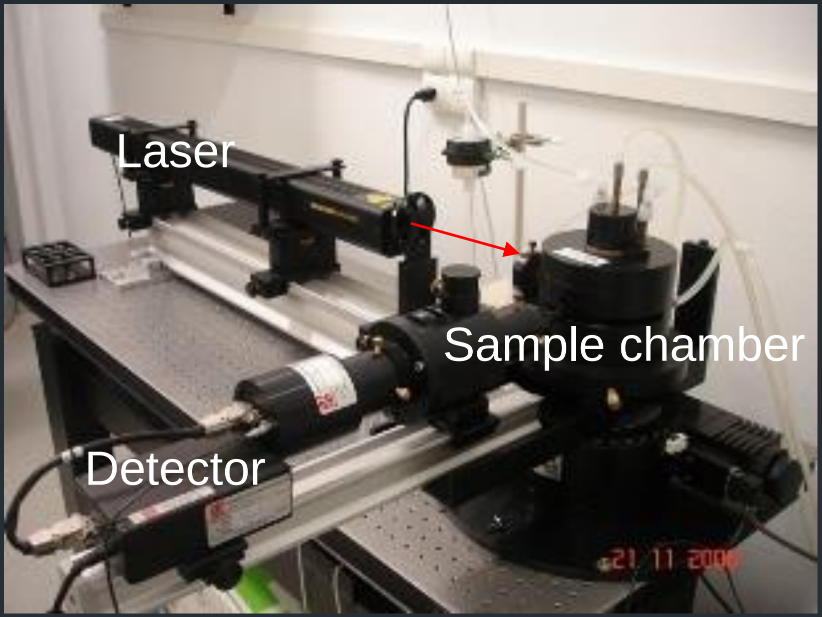
Light Scattering: some useful rules of thumb:

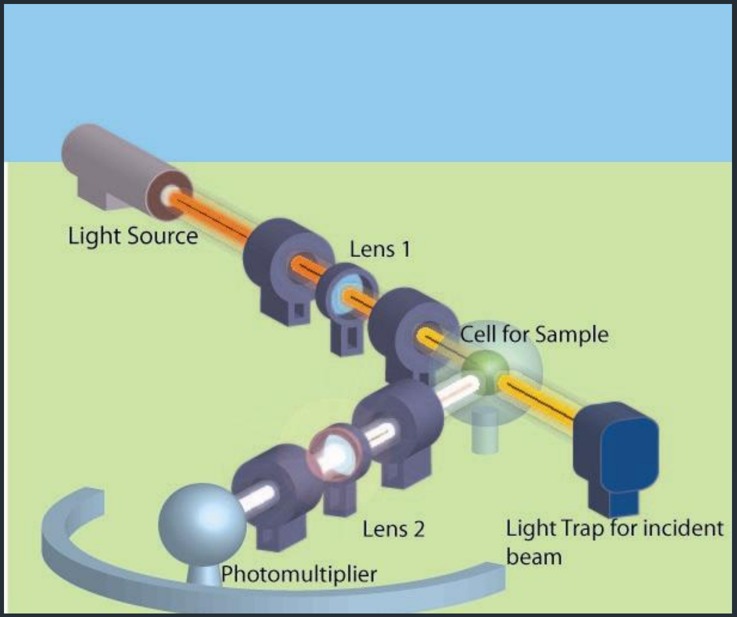
Scattering cross section angular dependance with particle size



Backscattering detection prevents from multiple scattering (concentrated samples) and allows to detect small particles in presence of bigger ones

DLS equipments until today:SLS/DLS bench with goniometer





- Adjustable scattering angle
- Several detectors
- Static and Dynamic Light Scattering
- Cross correlation
- Particle size and Molecular weight measurements
- Mainly for diluted samples
- Expensive and large dimensions

Modern DLS equipments :

Disposable cell

Embedded cell

- size range : from 1nm up to 10µm
- Mature and standardized method (ISO 13321 (1996) & ISO 22412 (2008)
- Bench top configuration: solutions dedicated to laboratory analysis
- Fast and relatively cheap compare to TEM and SAXS!
- But not fitted for process and in situ measurement!!!

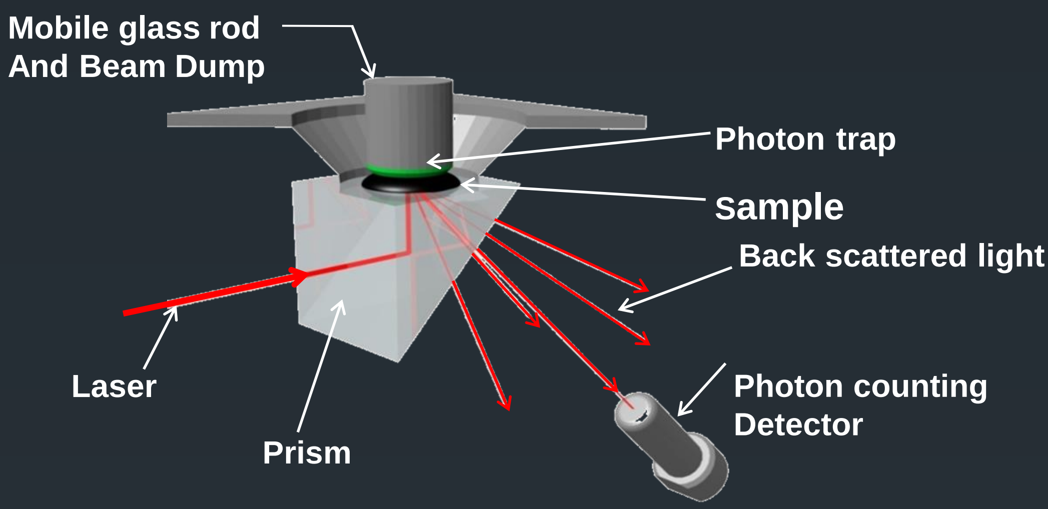
VASCO™

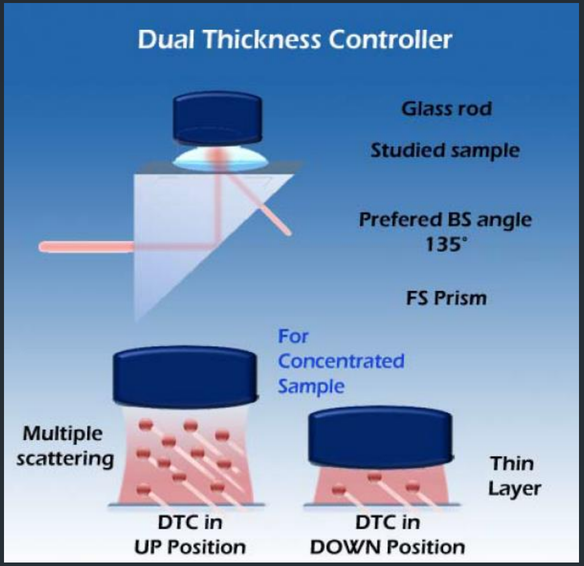
Batch Measurements

Opaque & concentrated media

Vasco particle size analyzer: a unique sample Cell design

The thin layer analysis mode





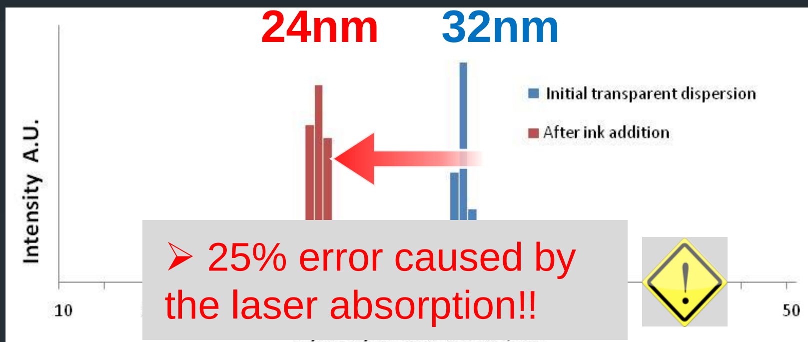
- Innovation in the sample cell configuration: Dual Thickness Control (DTC- patented)
- Thin layer analysis: prevents the sample from local heating and multiple-scattering.
- Backscattering detection (135°): low multiple scattering, better contrast for small particles
- Higher detection efficiency in opaque media.
- Solvent-proof cell measurement without consumables
- Proprietary inversion algorithm allowing efficient size distribution analysis
- Technology transfer from the French Institute of Petroleum

Common DLS artefacts and DTC benefits:

➢ Measurement of dark /opaque media

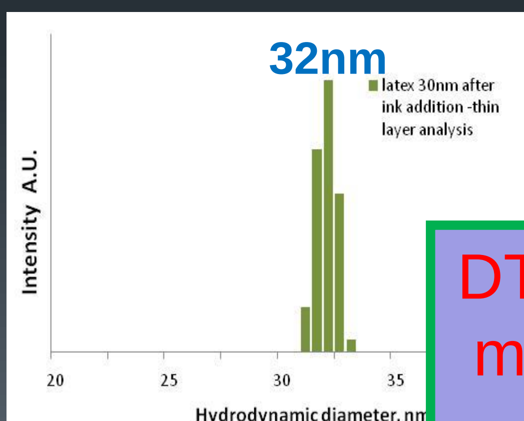
*A standard polystyrene latex (Ø=**30nm** by TEM) is mixed with black soluble ink (10wt%).*

Without DTC



➢ 25% error caused by the laser absorption!!

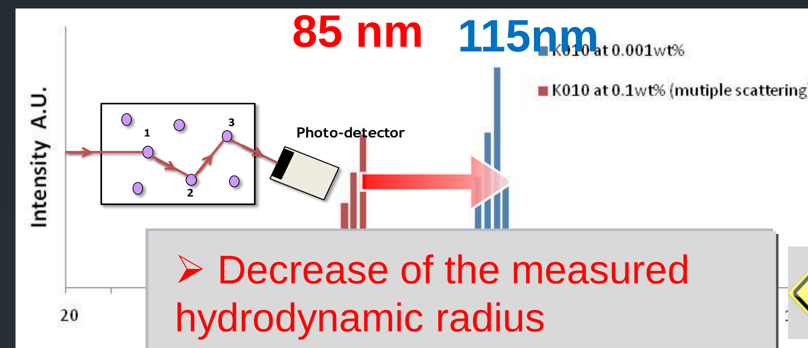
With DTC



➢ Measurement of concentrated samples

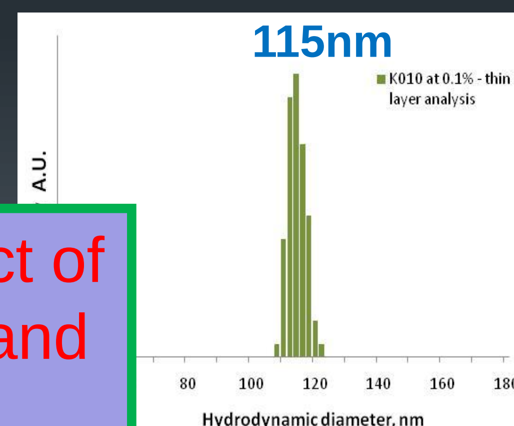
*A standard polystyrene latex (Ø=**100nm** by TEM) measured at 0.1 wt%*

Without DTC



➢ Decrease of the measured hydrodynamic radius

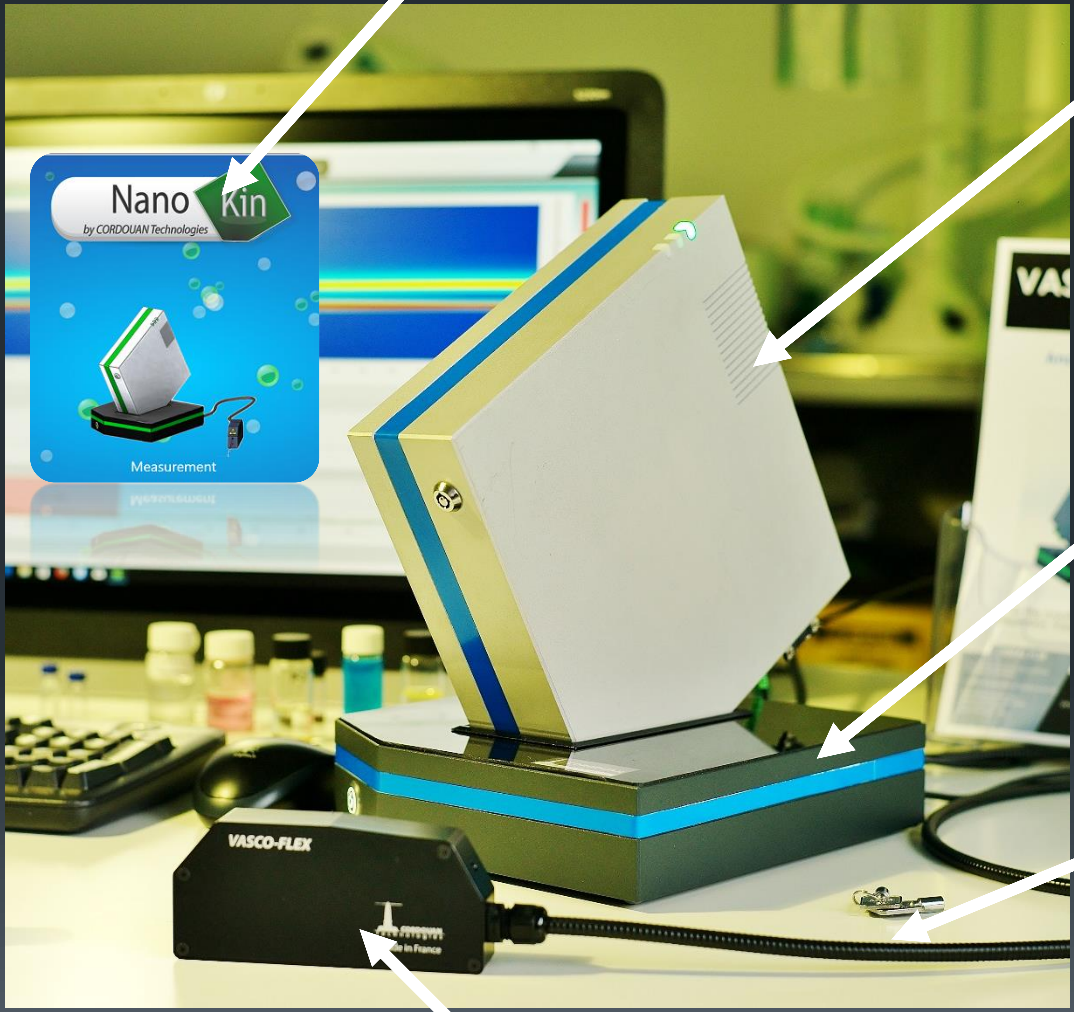
With DTC



DTC reduces impact of multiple scattering and light absorption

VASCO KIN: In Situ Time Resolved Nanoparticle Size Analyzer

Dedicated software



Optical unit

- Fast acquisition electronics
- APD detector
- Laser source

Control unit

- computer
- power supply

Optical fiber umbilical

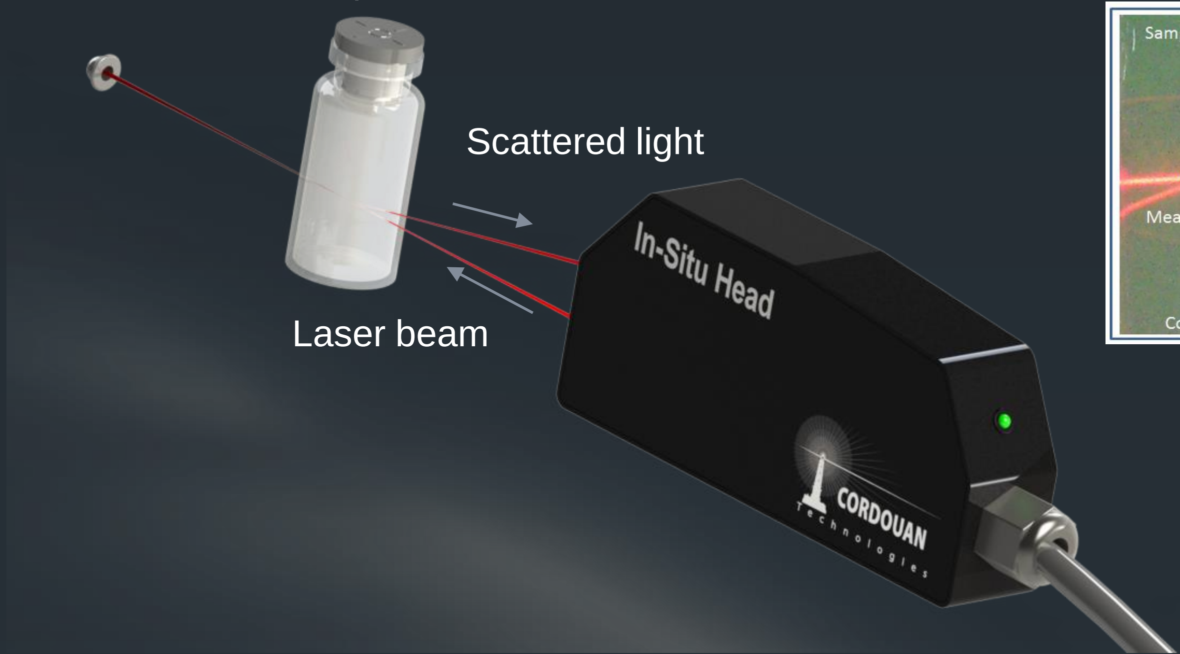
In situ remote probe

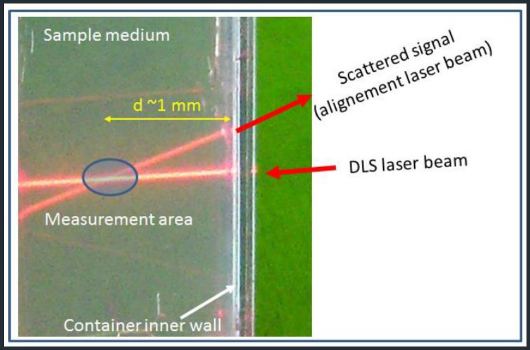
In situ head concept: the power of DLS, the flexibility of Optical fiber

A change of paradigm: *“bring your measurement to your process!”*

- Non invasive, no need to bacth the sample
- Adjustable working distance /scattering angle
- Alignment laser for easy installation
- High accuracy remote temperature sensor
- Easy maintenance
- Ideal for measurements in glass capillaries, or in situ

In Situ fibre remote head principle





Features:
- Non invasive
- Small footprint
- Adjustable working distance /scattering angle
- Alignment laser for easy installation
- High accuracy remote temperature sensor
- Flexibility and upgradability : easy switch between options
- Easy maintenance
- Ideal for measurements in glass capillaries, or in situ

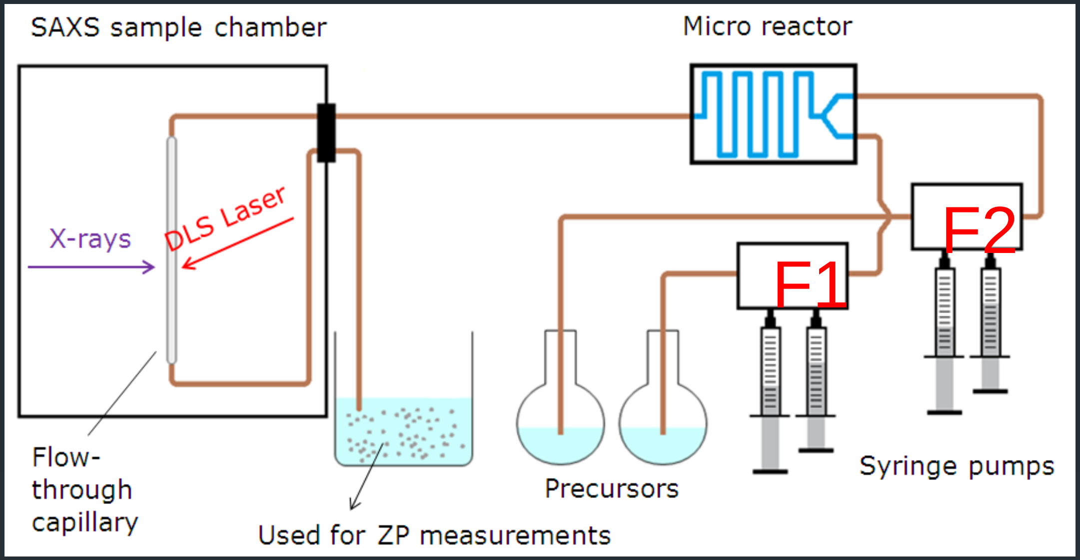
Application Examples

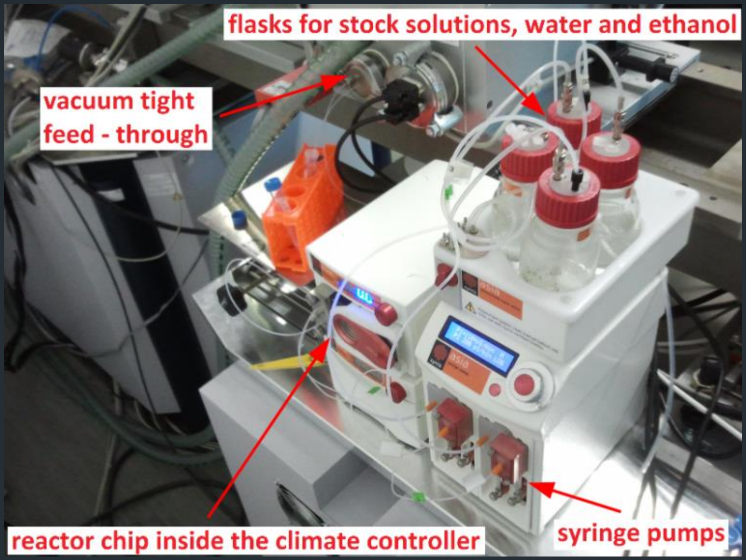
Example 1

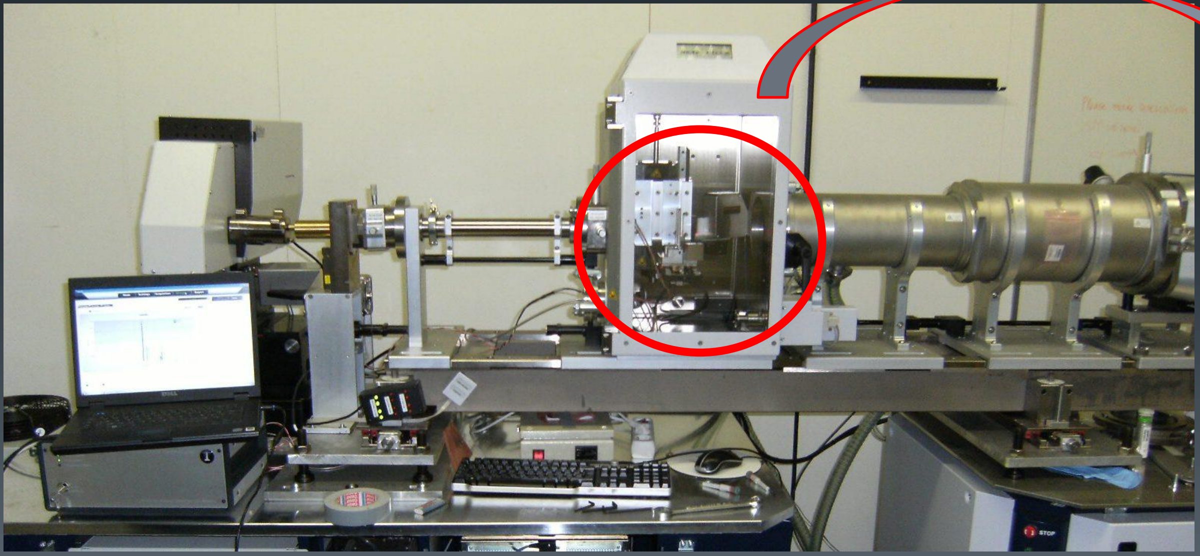
Combined Remote DLS & High flux SAXS for NPs synthesis monitoring

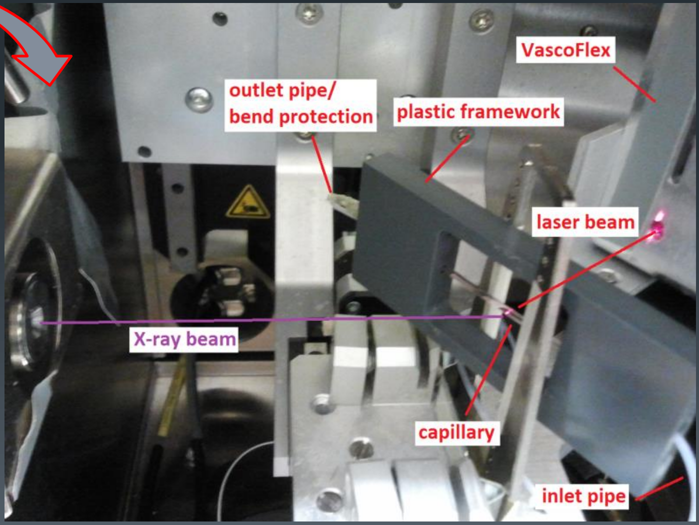
SNOW CONTROL FP7 Project

Combined Remote DLS & High flux SAXS for NPs synthesis monitoring





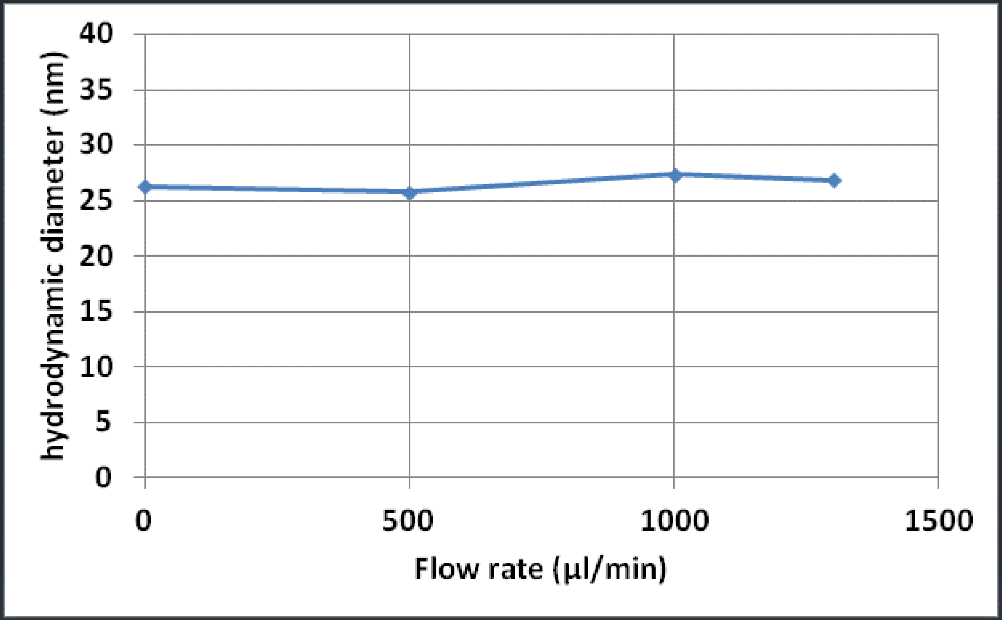




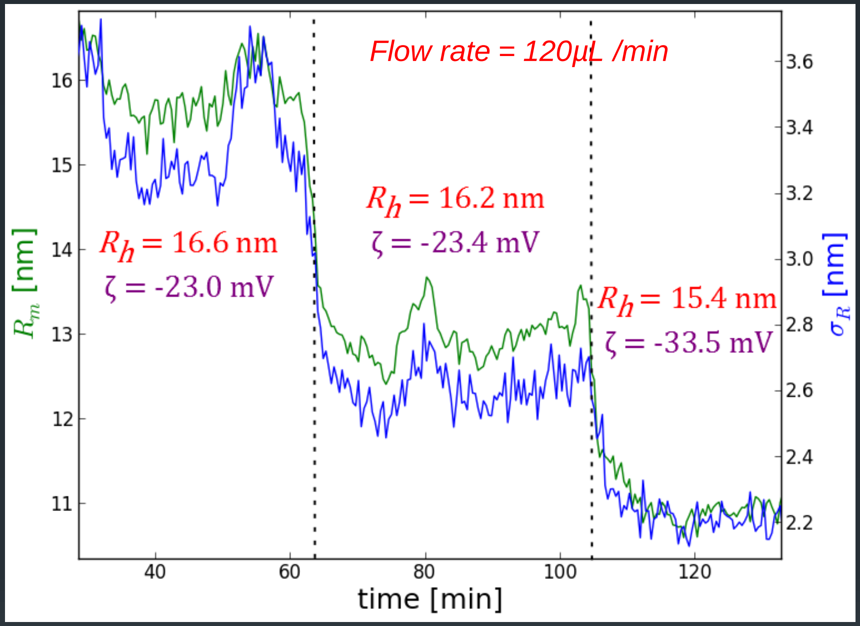
On line SiO2 NPs synthesis monitoring

Hydrolysis –condensation method : TEOS in Ethanol (F1) + NH3 in H2O (F2)

Impact of flow rate (F1+F2)



Impact on precursors mixing ratio (F1/F2)



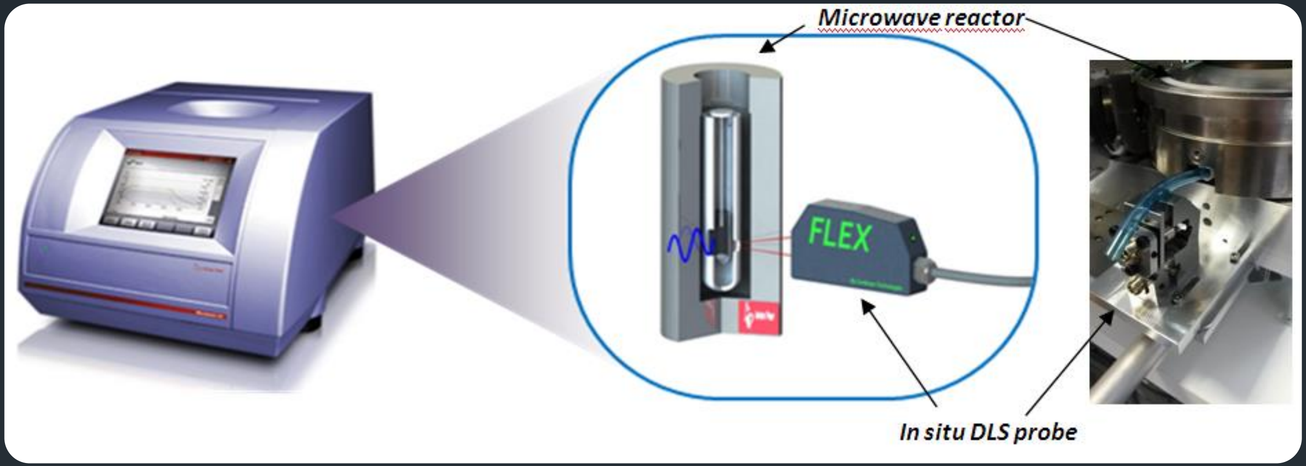
- Consistent results between SAXS and DLS measurements
- Allow to track and tune synthesis process in an accurate way

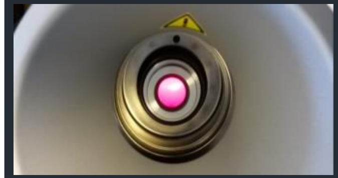
Example 2

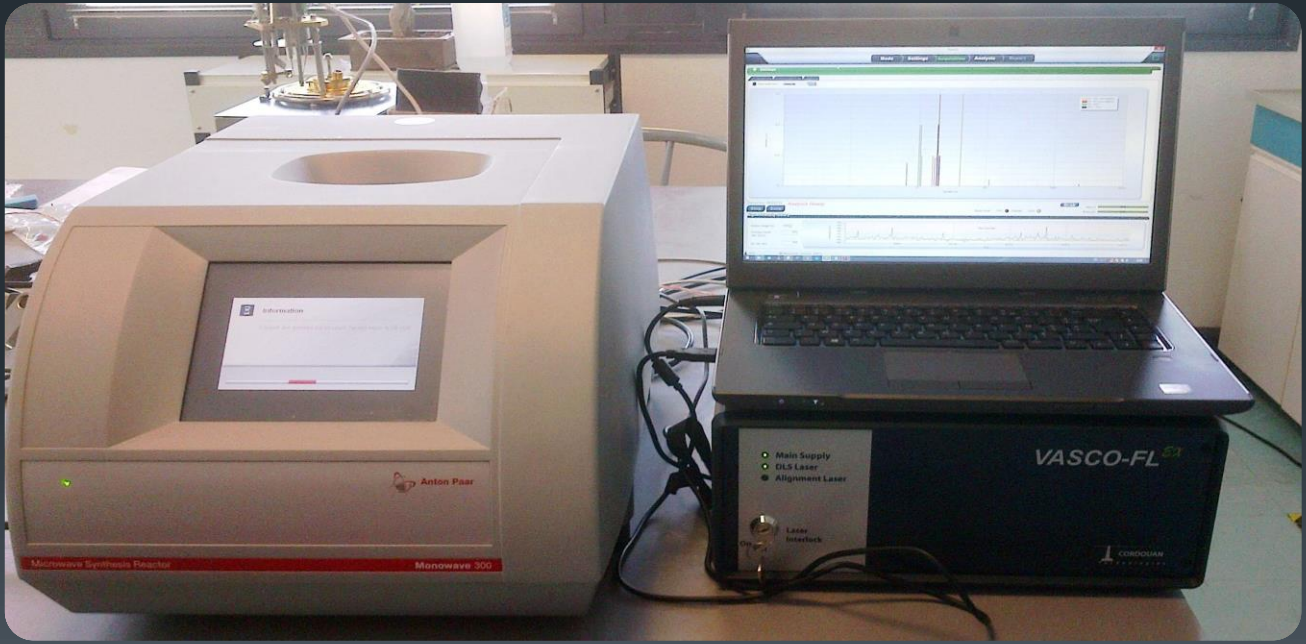
In situ kinetics monitoring
of Microwave assisted NPs synthesis

Anton Paar

In situ kinetics monitoring of Microwave assisted NPs synthesis



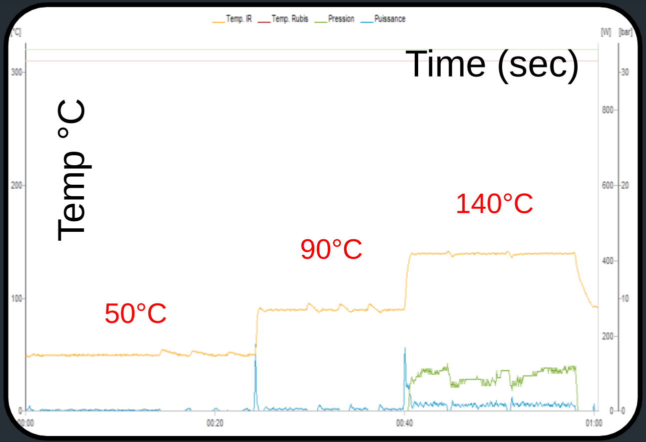


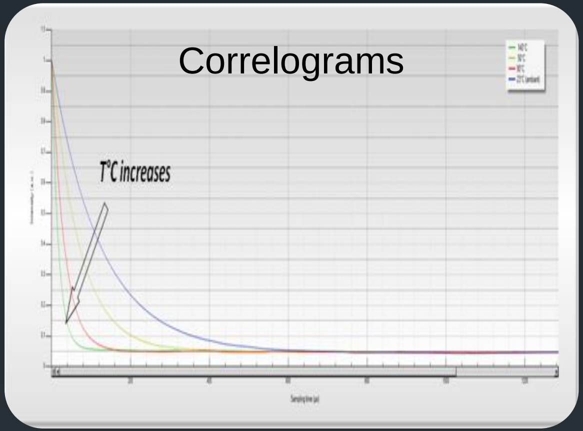


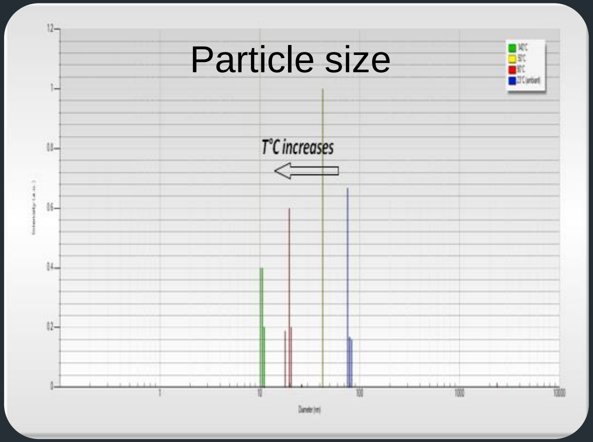
- In situ DLS successfully integrated into a commercial microwave reactor
- Under test and qualification at the College de France-Paris

Real-time & In situ monitoring of Microwave assisted NPs synthesis

Validation tests done on SiO2 slurries







True temperature	Corresponding Viscosity (cP)	Corrected Averaged size (nm)
50°C	0.55	**76**
90°C	0.3	**72**
140°C	0.196*	**68**

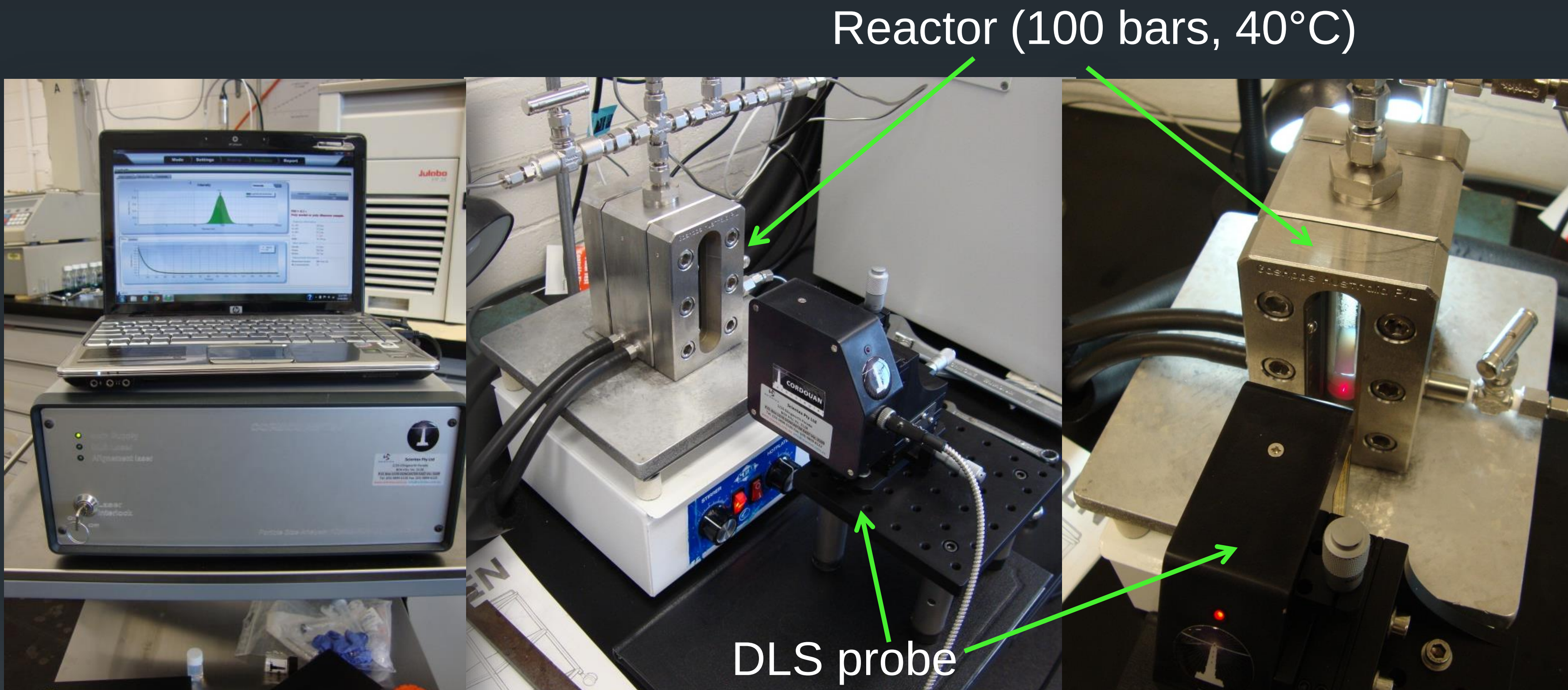
- Very consistent an d reproducible results
- 1st demonstration ever done opening up new possibility on NP synthesis monitoring

Example 3

Particle Size Measurement inside supercritical CO_2 synthesis reactor

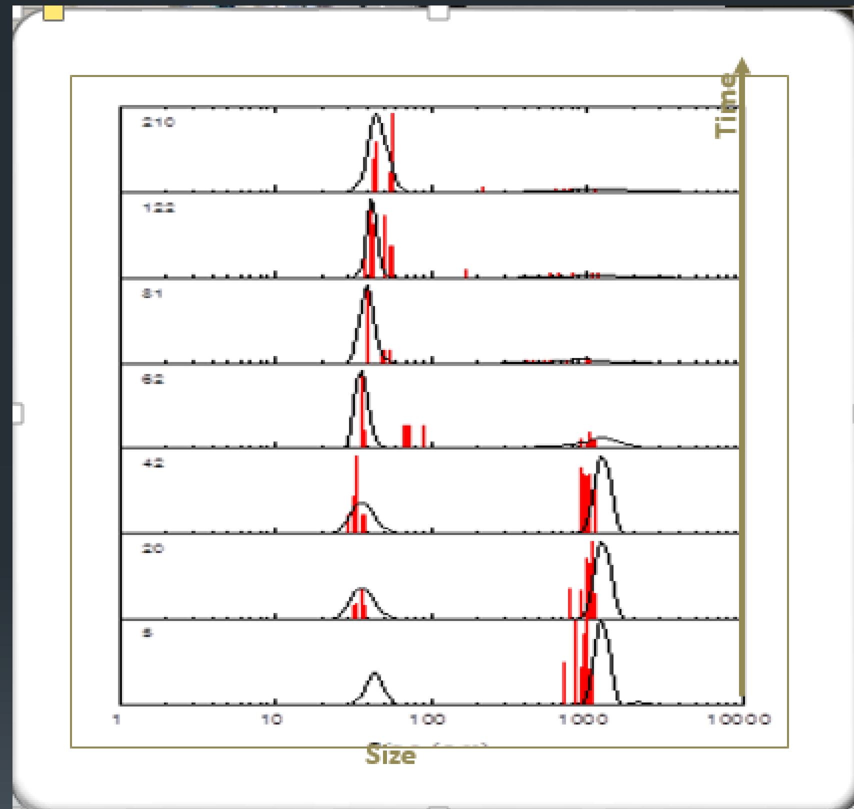
UNSW
AUSTRALIA

Particle Size Measurement inside supercritical CO_2 synthesis reactor



Particle Size Measurement in supercritical CO_2 synthesis reactor

- 10 wt% styrene rel. to system, 10 wt% Dowfax 8390 (surfactant) rel. to monomer, 8 wt% Hexa Decane rel. to styrene
- Sonicated for 10 min, 65% input intensity
- CO_2 is used to control the size of nano-emulsion droplets



- Use DLS measurements to correlate turbidity variation with particle size
- Implement accurate control of the size of monomer droplets/NP

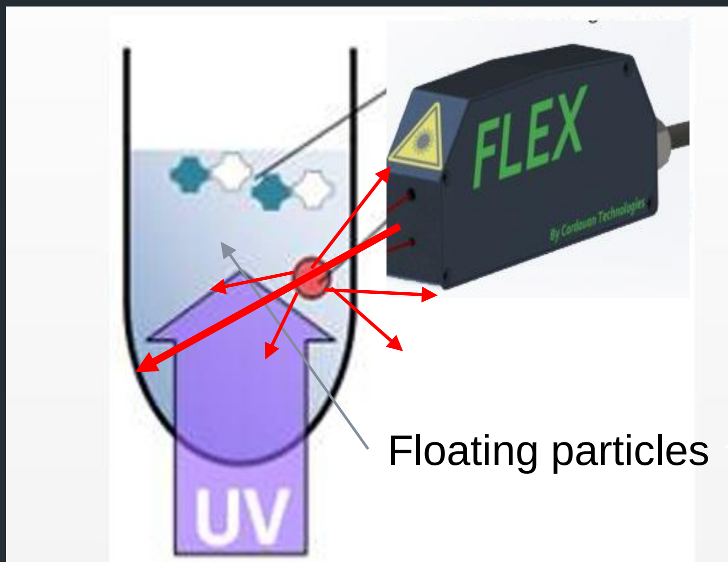
Example 4

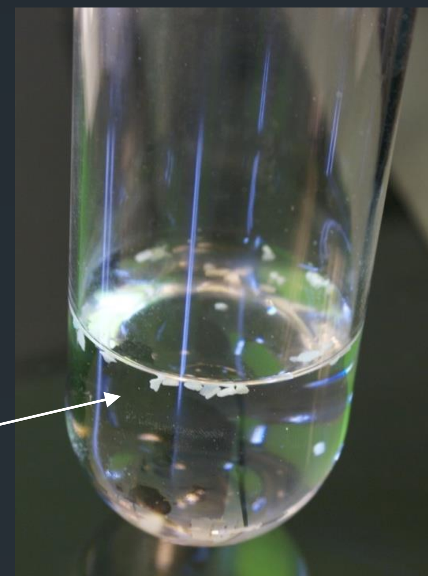
Environmental application: Nano Plastic detection in Ocean water

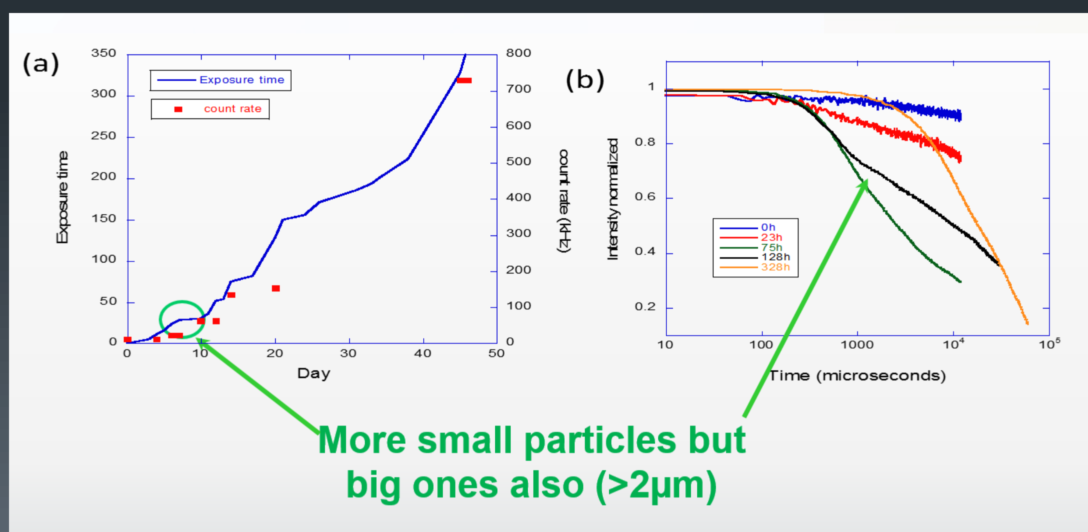
EXPÉDITION
7e CONTINENT

Environmental study : Evidence of Plastic Nps in Ocean

Lab study of Plastic NPs formation under oceanic like UV insolation conditions



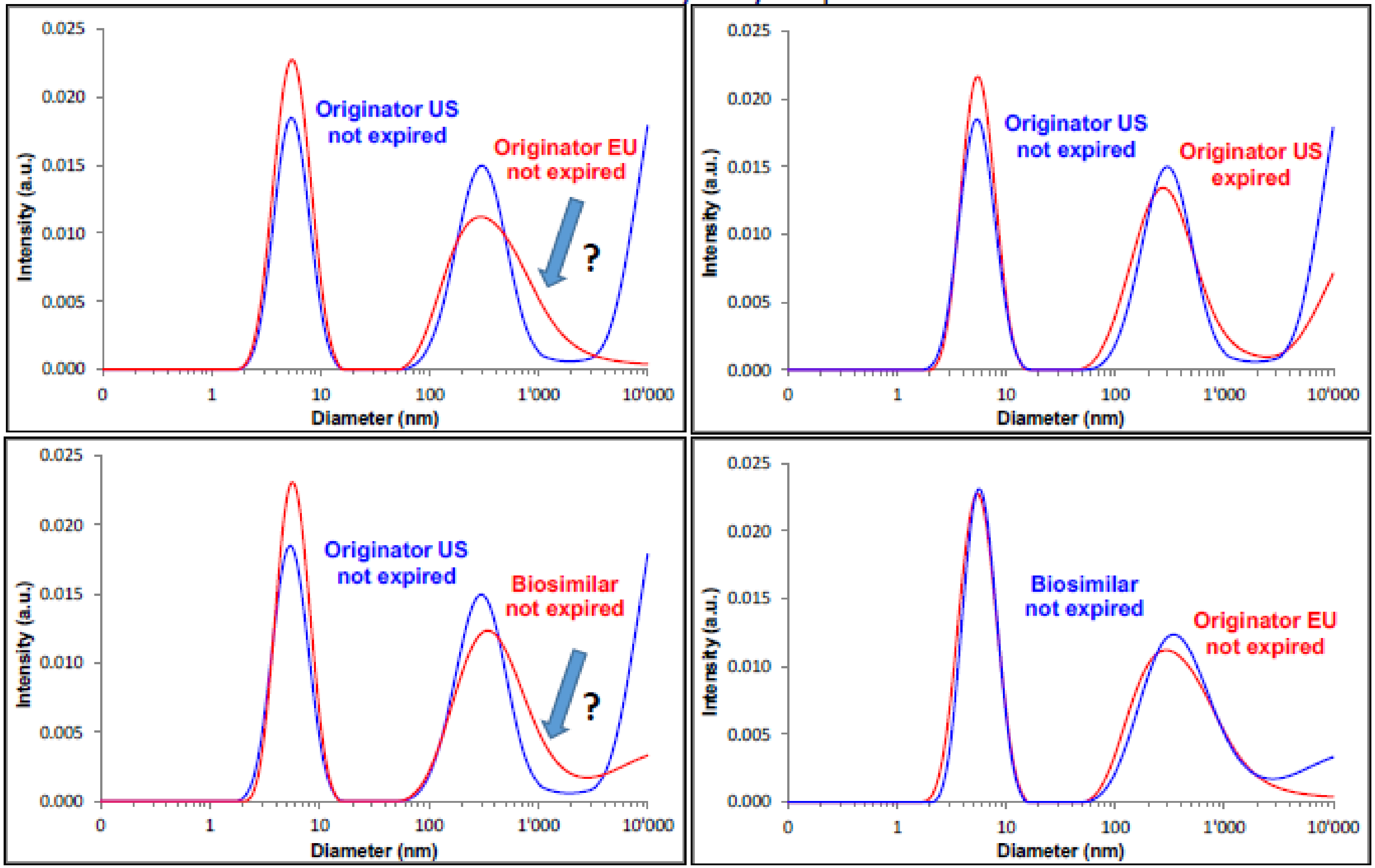




Example 5

Measurement in Bio pharma injectable

THERAPEOMIC, INC., not published data

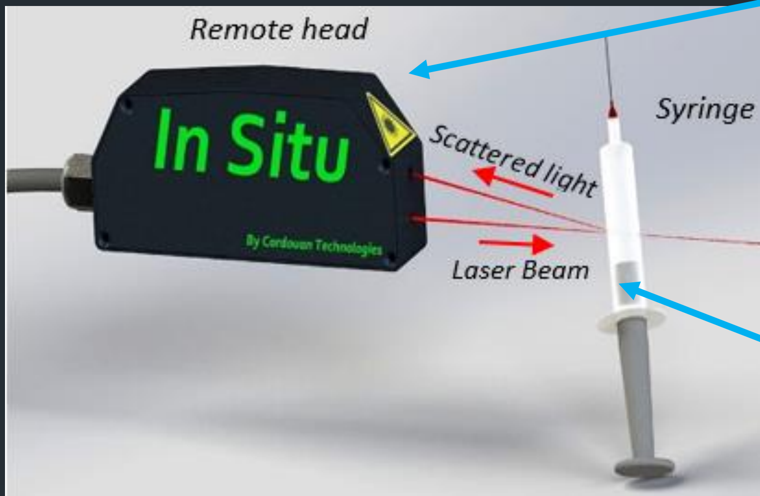


	Intensity mode		Number mode
	Ø (nm) Peak 1	Ø (nm) Peak 2	Ø (nm) Peak 1
Originator US not expired	**5.4 ± 0.1**	**299 ± 27**	**2.7 ± 0.2**
Originator EU not expired	**5.4 ± 0.1**	**293 ± 11**	**2.7 ± 0.2**
Biosimilar not expired	**5.7 ± 0.1**	**340 ± 27**	**3.2 ± 0.2**
Biosimilar expired	**5.8 ± 0.2**	**306 ± 38**	**3.1 ± 0.4**
Originator US expired	**5.5 ± 0.2**	**262 ± 37**	**3.0 ± 0.1**

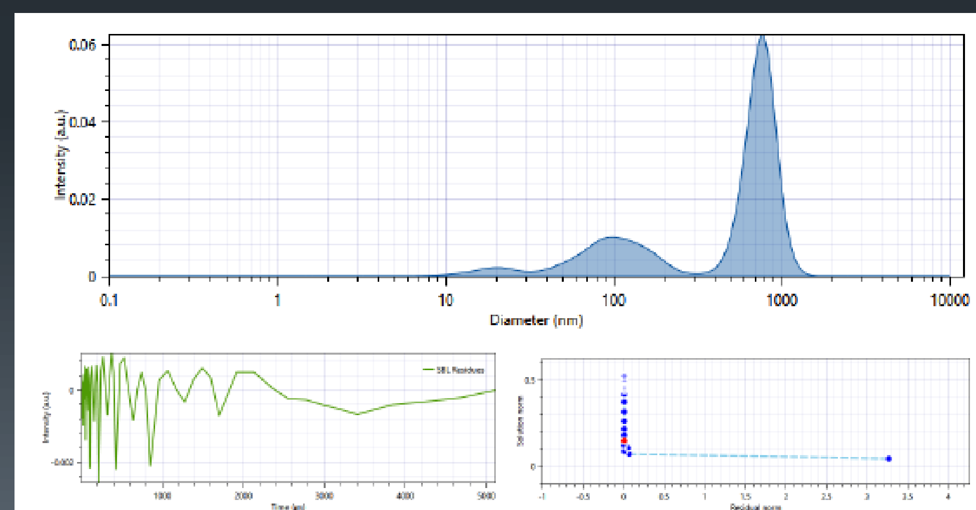
Darpin, G., Poirier, E., Arvinte, T. (2018) not published data

Prelimiray measurements on Flew injectable vaccines

Remote probe



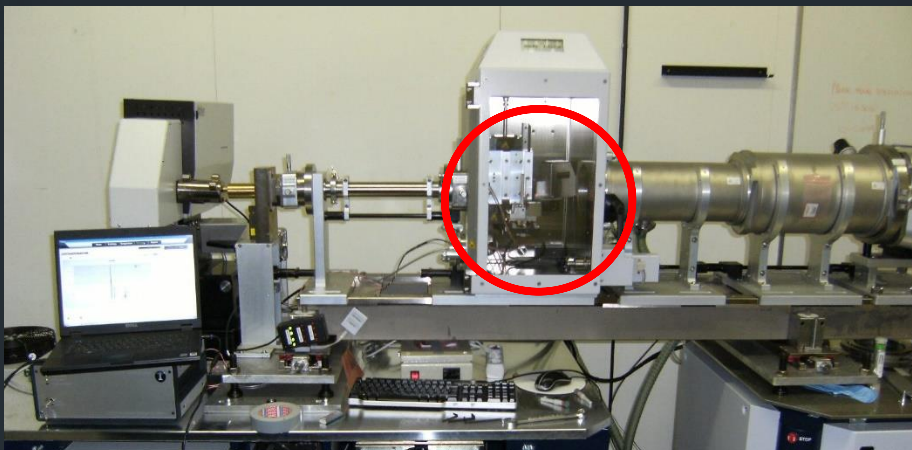
Injectable syringe



Other examples…

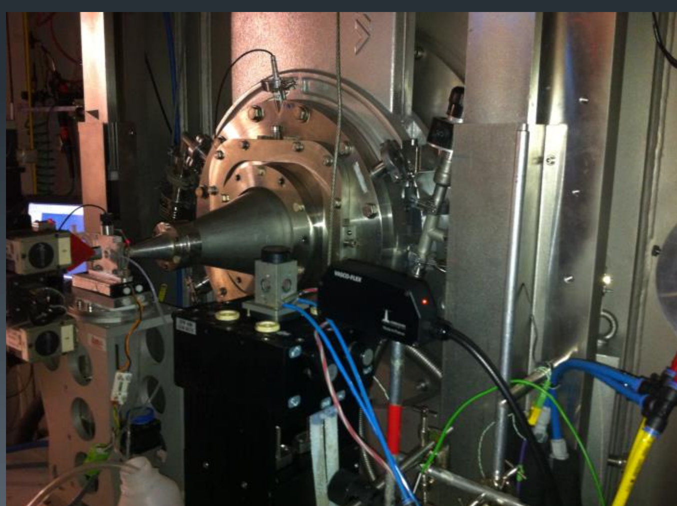
Examples of instrumental coupling

with SAXS instrument

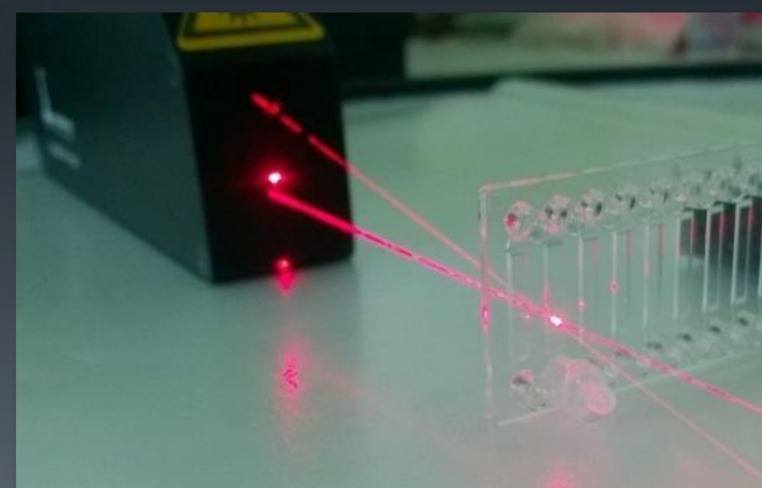


with crystalization reactors

With SANS/SAXS Lines



to µfluidics chips



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- Hunter R, Zeta potential in colloidal science; Academic press, New York, 198
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- Combining SAXS and DLS for simultaneous measurements and time-resolved monitoring of nanoparticle synthesis; A. Schwamberger & al, Nuclear Instruments and Methods in Physics Research B 343 (2015) 116–122
- Structure and Dynamic Properties of Colloidal Asphaltene Aggregates; Joëlle Eyssautier & al; *Langmuir*, 2012, 28 (33), pp 11997–12004 - American Chemical Society
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